Scoping Review Title: Scoping Review of Neuromonitoring practices for neonates with congenital heart disease

Researchers:
Andrea C. Pardo, MD[1], Denise Nunes[2], Melisa Carrasco, MD, PhD[3], Dawn Gano, MD[4], Vann Chau MD[5], Valerie Chock, MD[6], Pia Wintermark, MD[7], Shawn Sen, MD [8], Courtney J. Wusthoff, MD MS[9]

Affiliations:
1.Department of Pediatrics (Neurology and Epilepsy). Northwestern University Feinberg School of Medicine. Chicago, IL.
2. Galter Health Sciences Library. Northwestern University Feinberg School of Medicine. Chicago, IL.
3.Department of Neurology. University of Wisconsin School of Medicine and Public Health. Madison, WI.
4. Department of Neurology and Pediatrics, University of California, San Francisco, San Francisco, CA
5. Department of Pediatrics (Neurology), The Hospital for Sick Children, SickKids Research Institute (Neuroscience and Mental Health) and University of Toronto, Toronto, Canada
6. Department of Pediatrics (Neonatology), Lucile Packard Children's Hospital and Stanford University. Palo Alto, CA.
7. Department of Pediatrics, Faculty of Medicine and Health Sciences, McGill University. Montreal, Canada.
8.Department of Pediatrics (Neonatology). Northwestern University Feinberg School of Medicine. Chicago, IL.
9. Department of Neurology, Stanford University. Palo Alto, CA.

Introduction: The global reported incidence of congenital heart disease is high up to a 9.410 per 1000 births and is steadily increasing(1). There is a high rate of neurologic complications associated to CHD that affect the lifespan(2-5). Neonates with congenital heart disease are likely to have seizures in the postoperative period(6). Rates of seizures in neonates with congenital heart disease have been reported in approximately 10%, of which the majority are subclinical(7). At present, the neurocritical care of neonates with congenital heart disease is not standardized. A recent survey has identified the use of neuromonitoring techniques such as electroencephalogram (EEG), including amplitude-integrated EEG (aEEG), and near infrared spectroscopy (NIRS) as areas of high institutional variability and areas of deep need for further study(8). Specifically, neuromonitoring practices remain variable and the impact of these practices for the care of neonates with CHD remains unknown. The American Clinical Neurophysiology Society has identified neonates with congenital heart disease, at risk for acute brain injury and neonatal encephalopathy as a high-risk population for which neuromonitoring should be implemented, the Neonatal Cardiac Care Collaborative supported these recommendations(9, 10).

Rationale: At present, the neurocritical care of neonates with congenital heart disease is not standardized. A recent survey has identified the use of neuromonitoring techniques such as electroencephalogram (EEG), including amplitude-integrated EEG (aEEG), and near infrared spectroscopy (NIRS) as areas of high institutional variability and areas of deep need for further study(8). Specifically, neuromonitoring practices remain variable and the impact of these practices for the care of neonates with CHD remains unknown. The American Clinical Neurophysiology Society has identified neonates with CHD as a high-risk population for acute brain injury and neonatal encephalopathy and suggests continuous EEG monitoring after cardiopulmonary bypass. The Neonatal Cardiac Care Collaborative supported these recommendations(9, 10). Yet, there are no scoping or systematic reviews that evaluate the known literature for neuromonitoring of neonates with CHD.

Objectives: We seek to synthesize the known literature for neuromonitoring with EEG, aEEG, NIRS, transcranial doppler (TCD) and other multimodal neuromonitoring techniques for neonates with congenital heart disease to clarify current practices, document available studies, investigate gaps in research that may inform the care of this population. This review serves as part of a wider work in which stakeholders (Newborn Brain Society as well as content experts) are formally engaged in a separate qualitative research process, examining their views, experiences, and opinions of neurocritical care for the neonate with congenital heart disease.

Methods:
This study will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA- ScR)(11) as recommended by the Joanna Briggs Institute (JBI) and PRISMA-ScR reporting guidelines. The methodology, inclusion, exclusion criteria and data extraction proforma were reviewed by the Newborn Brain Society Guidelines and Publications Committee members for additional feedback. The search strategies were drafted by an experienced academic medical librarian (DN) and further refined through team discussion. The following databases will be queried: Ovid, EmBase, Web of Science and Cochrane. Unlike systematic reviews, scoping reviews do not require an antecedent protocol registration(11), notwithstanding, review objectives, eligibility criteria, and preliminary study characteristics to be extracted were determined a priori and registered into Galter Library Digital Hub, Northwestern Medicine's institutional repository(12). The search results will be exported into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). All results titles, abstracts and full text will be reviewed by seven authors on the team (AP, MC, DG, VC, PW, SS, VC). Any discrepancies will be reviewed by two authors to make a final decision about study inclusion and review for bias (CW, AP).

The inclusion criteria were selected in accordance to our research question- what are the current neuromonitoring practices for neonates with congenital heart disease?

Inclusion Criteria
***P**opulation-*
Neonates (< 30 days of age)
Term and preterm

***I**ntervention-*
Electroencephalogram (EEG) including routine and continuous EEG
Amplitude Integrated Electroencephalogram (aEEG)or Cerebral Function Monitoring (CFM)
Near Infrared Spectroscopy
Transcranial Doppler
Multimodal monitoring (use of more than 2 modalities of monitoring)

***C**ontext- congenital heart disease terms:*
Single Ventricle Physiology, Hypoplastic left heart, transposition of the great arteries, truncus arteriosus, aortic valve stenosis, aortic coarctation, hypoplasia or interruption (left ventricular outflow tract and/or aortic arch obstruction)

Study design- we will include RCT, retrospective reviews, prospective cohorts and other studies using other experimental designs, from 1990- until the present date.

Exclusion criteria- abstracts, conference proceedings, case reports, editorials, letters and other narrative reviews. Articles written in languages other than English that are unable to be translated.

Information sources: We will search published literature from the following electronic databases to identify relevant studies: Ovid (Medline), Embase (Elsevier), Web of Science and Cochrane Database of Systematic Reviews (Wiley).

Search: Search terms and strategies will be developed closely with an experienced librarian (DN). The search strategy will combine keywords and controlled vocabulary terms for the following concepts: infants, congenital heart diseases and neuromonitoring. We will develop the search in Medline (OVID) and adapt it to the pre-specified databases. A draft of our search strategy created in Medline (OVID) is provided below:

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions <1946 to March 03, 2023>		
1	exp Infant, Newborn/	667662
2	((Infant* and (preterm or term or premature or postmature)) or (Newborn* or Neonat*)).ti,ab.	486263
3	1 or 2	883859
4	exp Heart Defects, Congenital/	167822
5	exp Aortic Coarctation/	9790
6	exp Aortic Valve Stenosis/	50446
7	exp Hypoplastic Left Heart Syndrome/	2816
8	exp "Transposition of Great Vessels"/	8270
9	exp Truncus Arteriosus/	287
10	exp Univentricular Heart/	203
11	(((congenital adj2 (heart or cardiac)) and (disease* or defect* or abnormal* or malformation*)).ti,ab.	255844
12	("Single Ventricle Physiology" or "Hypoplastic left heart" or "transposition great arteries" or "truncus arteriosus" or "aortic valve stenosis" or "aortic coarctation" or "hypoplasia or interruption" or "left ventricular outflow tract" or "aortic arch obstruction" or "Univentricle heart").ti,ab.	18982
13	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	425433
14	exp Neurophysiological Monitoring/	2210
15	exp Diagnostic Techniques, Neurological/	435902
16	(Monitor* adj3 (brain or cerebral or multimodal or neonatal or neuro* or noninvasive or optical)).ti.	5546

17	("amplitude integrated electroencephalography" or "cerebral blood flow" or "cerebral hemoglobin oxygenation" or "cerebral near-infrared spectroscopy" or " cerebral near infrared spectroscopy" or "cerebral function monitor" or " cerebral oximetry electroencephalograph*" or EEG or "metabolic brain measurement*" or "Near-infrared spectroscopy" or "near infrared spectroscopy" or NIRS or "transcranial Doppler").ti,ab.	143003
18	14 or 15 or 16 or 17	505658
19	3 and 13 and 18	791
20	limit 19 to yr="1990 -Current"	702

Selection of sources of evidence: The search results will be exported into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). All results titles, abstracts will be screened by AP and MC, and full text will be reviewed by seven authors on the team (AP, MC, DG, VC, PW, SS, VC). Any discrepancies will be reviewed by two authors to make a final decision about study inclusion and review for bias (CW, AP).

Data charting process: Data will be charted on a previously drafted data proforma. Appendix 1.

Data items: Study design, study objective, number of patients, type of congenital heart disease, neuromonitoring modality, duration of monitoring if available, outcome associations if available.

Critical appraisal of individual sources of evidence: Critical appraisal of the articles will be done in accordance to JBI guidance to critically appraise evidence depending on study type and documented in the study proforma in a summative statement (13, 14).

Synthesis of results: Data will be summarized according to neuromonitoring modality.

Appendix 1. Data characterization proforma

A. Authorship characteristics		
Variable	**Category**	**Explanation**
Author(s)	☐ _____	Please list.
Year of Publication	☐ _____	Please state.
Country	☐ _____	Please state the setting where the study took place.

B. General Study Characteristics		
Variable	**Category**	**Explanation**
Study design	☐ Case series ☐ Cohort ☐ Case Control ☐ Randomized controlled trial	Please select.
Objective(s)	☐ _____ _____	Please briefly describe.
Population size	☐ _____	Please state.
Major sources of bias		Please state

C. Description of Congenital Heart Disease		
Variable	**Category**	**Explanation**
Type of Congenital Heart Disease	☐ Single Ventricle Physiology ☐ Transposition of the great arteries ☐ Truncus arteriosus ☐ Coarctation of the aorta ☐ Left ventricular outflow obstruction _____	

D. Description of Neuromonitoring utilized		
Variable	**Category**	**Explanation**
Format of technology	☐ Electroencephalogram (EEG) ☐ amplitude integrated EEG (aEEG) ☐ Near Infrared Spectroscopy ☐ Transcranial Doppler ☐ Multimodal monitoring (>2 methods).	Please select all that apply.
Outcome measure(s) / assessment(s) / instrument(s) employed in study	☐ _____	Please briefly describe.
Duration of neuromonitoring study	☐ _____	Please state.
Indications for neuromonitoring study	☐	Please state.

E. Major findings		
Variable	**Category**	**Explanation**
Major findings	☐ _____ _____ _____	Please describe.
Major challenges	☐ _____ _____	Please describe.

References

1. Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019;48(2):455-63.
2. Bolduc ME, Dionne E, Gagnon I, Rennick JE, Majnemer A, Brossard-Racine M. Motor Impairment in Children With Congenital Heart Defects: A Systematic Review. Pediatrics. 2020;146(6).
3. Kordopati-Zilou K, Sergentanis T, Pervanidou P, Sofianou-Petraki D, Panoulis K, Vlahos N, et al. Neurodevelopmental Outcomes in Tetralogy of Fallot: A Systematic Review. Children (Basel). 2022;9(2).
4. Massaro AN, El-Dib M, Glass P, Aly H. Factors associated with adverse neurodevelopmental outcomes in infants with congenital heart disease. Brain & development. 2008;30(7):437-46.
5. Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, et al. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. Circulation. 2012;126(9):1143-72.
6. Clancy RR, Sharif U, Ichord R, Spray TL, Nicolson S, Tabbutt S, et al. Electrographic neonatal seizures after infant heart surgery. Epilepsia. 2005;46(1):84-90.
7. Naim MY, Gaynor JW, Chen J, Nicolson SC, Fuller S, Spray TL, et al. Subclinical seizures identified by postoperative electroencephalographic monitoring are common after neonatal cardiac surgery. The Journal of thoracic and cardiovascular surgery. 2015;150(1):169-78; discussion 78-80.
8. Leon RL, Levy PT, Hu J, Yallpragada SG, Hamrick SEG, Ball MK, et al. Practice variations for fetal and neonatal congenital heart disease within the Children's Hospitals Neonatal Consortium. Pediatric research. 2022.
9. Shellhaas RA, Chang T, Tsuchida T, Scher M, Riviello JJ, Abend NS, et al. Neonatal EEG Monitoring Consensus Statement. 2011.
10. Ortinau CM, Smyser CD, Arthur L, Gordon EE, Heydarian HC, Wolovits J, et al. Optimizing Neurodevelopmental Outcomes in Neonates With Congenital Heart Disease. Pediatrics. 2022;150(Supplement 2).
11. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Annals of Internal Medicine. 2018;169(7):467-73.
12. Library GHS. Digital Hub [Available from: https://digitalhub.northwestern.edu.
13. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: Systematic reviews of etiology and risk JBI2020. Available from: https://synthesismanual.jbi.global.
14. Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, et al. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. JBI Evid Synth. 2020;18(10):2127-33.