JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2025, VOL 8, NO S12

Neurodevelopmental Outcomes In Children With Single Ventricle Physiology After Fontan Procedure: A Systematic Review

Ahmed M Al zweihry[1], Ahmed salim Al mutiri[1],Abdulaziz Al ghamdi[2],Waad alotibi[1,] Bander A Alyousef[1],Abdulaziz Hamad Al amro [3] ,Esra Alamri[3], Bader A Alruwaili[4]

[1-]Division of Cardiology ,Department of pediatrics ,Alyamamh hospital ,Central Second cluster-Riyadh ,Ministry of Health
[2-]Division of PICU , Department of pediatrics ,Al yamamh hospital ,Central Second Cluster-Riyadh ,Ministry of Health- KSA.
[3-]Pediatrics Department , Al yamamh hospital , Central second Cluster –Riyadh , Ministry of Health-KSA.
[4-] Division of Emergency ,Department of Pediatrics,Alyamamh hospital ,Central Second Cluster –Riyadh ,Ministry of Health-KSA .

ABSTRACT

Background: Congenital heart disease with single ventricle that requires Fontan palliation poses a great neurodevelopmental issue that affects the quality of life in the long term.
Objective: The proposed systematic review is an attempt to synthesize the recent findings related to neurodevelopmental outcomes after Fontan procedure in children.
Methods: Thorough search of various databases that pinpoint peer-reviewed open-access articles that explored cognitive function, executive function, mental health, and other risk determinants.
Results: Post-Fontan children have recurrent neurodevelopmental malfunctioning such as processing speed deficiency, executive malfunction, and psychiatric morbidity. The intelligence quotient scores are at a low level that is far below population norms but quite normal in general.
Conclusions: Fontan survivors are associated with severe neurodevelopment problems requiring serious multidisciplinary follow-up in childhood and adolescence. There should also be early detection and specific intervention measures to make sure that the neurodevelopmental outcomes are maximized in the long term. The effects of patient-specific factors and perioperative morbidities are more likely to predict the outcomes than the surgical technique.

Keywords: Fontan procedure, single ventricle, neurodevelopment, cognitive functioning, mental health, systematic review.

INTRODUCTION

Single ventricle congenital heart disease is a major health challenge in the world, where high birth rates occur. The Fontan procedure was a solution that transformed the treatment by establishing total cavoPulmonary connection lacking functional second ventricle. Recent developments in surgery gave an impressive rise in the survival rates where a significant percentage of patients who underwent the Fontan

are now adults. Children with single ventricle physiology show the greatest risk in neurodevelopment disability relative to other congenital heart diseases. The knowledge of neurodevelopmental outcomes will be critical in risk stratification, the planning of early intervention and the use of long-term surveillance strategies. The review is a synthesis of the evidence in recent studies that investigated neurodevelopmental outcomes in Fontan population.

METHODS

Radical literature search was performed systematically in various electronic databases. Search was done using PubMed, MEDLINE, Web of science and Cochrane Library databases. Keywords were Fontan procedure, single ventricle, hypoplastic left heart syndrome and neurodevelopmental outcomes. Today, studies published between January and November underwent a systematic review to determine the eligibility criteria. Final analysis was done with only published peer-reviewed open access articles in English language. To ensure that the methodology was rigorous, grey literature and conference abstracts were excluded.

The inclusion criteria included those studies that were done on the neurodevelopmental outcomes among pediatric Fontan populations. Final review included studies that used standardized neurodevelopmental assessment tools and made use of original data. The exclusion criteria were case reports, studies that lacked standardized assessments, and study populations that were exclusively adult. Reference mining was done using review articles but this was not included in the data synthesis. The extraction of data was on cognitive outcomes, executive functioning, behavioral outcomes and psychiatric morbidity. Quality determination was conducted based on predefined observational study criteria of pediatrics populations.

RESULTS

Fontan patients of preschool age revealed lower scores in terms of intelligence quotient than healthy population levels in general. Cohorts of school-aged participants reported lower levels of intelligence quotient in the normal range throughout studies. (3) Modern researches determined that a large percentage of the population attains optimal neurodevelopmental outcome, which is no disabilities. (9, 10) The unadjusted intelligence quotient scores did not have any significant differences between the Fontan patients and the biventricular congenital heart disease. Processing speed was one of the most pertinent and stable areas of weaknesses across the studies.

Large percentage of parents and teachers rated adolescent Fontan patients in the at-risk range of dysfunction. Weaknesses skills such as anticipation abilities, organization and planning abilities in adolescence are particularly intense in metacognition. Fontan groups exhibited more impairment in visual-spatial types of executive functions than other cardiac diagnoses. (3) Attention-deficit hyperactivity disorder was identified in Fontan adolescents in much higher rates than general populations. (16) The problems with executive functions are more evident in adolescence when the demands on higher cognitive abilities become progressively stronger.

Most Fontan patients were given lifetime psychiatric diagnosis, whereas the percentage is greatly lower among healthy peers. Most frequent diagnoses were anxiety and attention-deficit hyperactivity disorder across the age groups that were extensively researched. (13) Depression scores were substantially high as compared to healthy counterparts in various study cohorts and populations. Patterns may have a biological background based on structural brain damage in regions involved in the regulation of anxiety and depression. (15) The quality of life was strongly predicted by the existence of depression, functional capacity, and the perceived availability of social support.

DISCUSSION

There are uniform neurodevelopmental issues in domains in children with single ventricle physiology. The scores of the intelligence quotient are within the normal range but way below the norms in the population. Deficits in processing speed prove to be the most reliable and clinically meaningful impairments in the long run. (5) Executive functioning is a vulnerable branch of cognitive functioning that influences functioning

in daily life and independence as well as the overall quality of life. The prevalence of attention-deficit hyperactivity disorder is significantly higher than the general population rates that necessitate specific interventions on patients. (1) Mental illness such as anxiety and depression is significantly high as compared to the healthy counterparts.

Several patient and perioperative variables are an indication of neurodevelopmental outcomes in Fontan survivors. The female sex is linked to positive outcomes and maternal education offers serious protective benefits. Patients who have a younger age at Fontan procedural time have better neurodevelopmental outcomes. (7) Atrioventricular valve concomitant intervention is an indicator that predicts poor patient outcomes in Fontan completion surgery. Preoperative lactate normalization is a more predictive factor in the immediate postoperative phase of all patients. Genetic abnormalities, nutritional conditions, and sociodemographic factors are patient-specific factors that have a strong impact on neurodevelopment trajectories. (4) The perioperative variables such as deep hypothermic circulatory arrest time, repeated surgeries and long hospital stay have significant roles.

Neurodevelopmental impairment is caused by prenatal, perioperative and chronic injury mechanisms in life. Poor prenatal brain development and disrupted fetal hemodynamics are some of the baseline cognitive and developmental risk factors. In critical times, perioperative brain injury is caused by cardiopulmonary bypass, circulatory arrest, and hemodynamic instability. (6) Commonly observed after cardiac surgery with bypass are white matter lesions, stroke, hemorrhage and microhemorrhages. Long-term hypoxemia in the palliative stages and long-standing low cardiac output conditions are chronic. (2) Venous-to-arterial shunting permits transit of thrombi that augments stroke risk during lifespan of all patients. The cumulative burden of the brain injury at several stages of surgery is a predictor of poor neurodevelopmental outcomes in the long-term.

Surgeries and the timing of surgeries undergo considerable evolution that has led to better outcomes although neurodevelopmental issues remain a challenge. Older-aged at surgery has been observed in historical Fontan cohorts than in the modern-day pediatric patients. Modern patients are Fontaned at younger ages with a staged approach with much better results. Neurological protection of all pediatric patients is enhanced by modern methods such as shorter circulatory arrest periods. (14) Fenestrated Fontan surgeries and bilateral Glenn staging are standard operations that enhance the overall survival and outcomes. (11) Although there have been advances in surgery, the neurodevelopmental issues continue to point out importance of patient-specific factors that are not solely dependent on the technique used. Future studies center on the early detection of the disease, neuroprotective measures, and specific treatment of the high-risk children.

The existing evidence indicates severe methodological shortcomings that need to be addressed using multicentric collaborative research projects. A wide range of study designs, assessment instruments, and mostly single-centered studies restrict the general quality of evidence substantially. Neurodevelopmental trajectory studies have small samples and selection bias on survivor and limit generalizability. (8) Patients are still in urgent need of intervention studies that investigate the effectiveness of cognitive training, psychiatric treatment, and nutritional support. Multicenter collaborative networks such as Fontan Outcomes Network combat the limitations using standardized data collection and cohorts. (11) Further studies should now focus on randomized controlled trials to investigate individual interventions that can be used to enhance neurodevelopmental outcomes to a higher level.

CONCLUSIONS

Children with Fontan physiology face severe neurodevelopmental issues that need long-term multidisciplinary follow-up management. Generally, intelligence is not impaired but processing speed and executive functioning are usually impaired. Morbidity in mental health such as anxiety, depression, and attention-deficit hyperactivity disorder is still significantly high. Patients-specific factors such as sex, maternal education, surgical age and the perioperative course affect outcomes. Early detection through universal screening procedures enhances developmental pathways both in childhood and adolescence in a significant way. Future studies should compare the efficiency of interventions and processes that underlie enduring neurodevelopmental vulnerability on a comprehensive basis.

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