5-2020

Complications and Management in Pediatric Heart Surgery

Hannah Berndt

Complications and Management in Pediatric Heart Surgery

Hannah D. Berndt

University of Arkansas

Abstract

The purpose of this literature review is to evaluate current research surrounding management of pediatric patients after cardiac surgery. Acute kidney injury (AKI) and neurodevelopmental deficits are the main discussion topics. This review analyzes the causes, risk factors, and effects of AKI. The diagnostic and management methods surrounding AKI are compared, and diagnostic approaches such as serum Cystatin C and fibroblast growth factor 23 are analyzed as potential future replacements to serum creatinine. The modality of renal replacement therapy is evaluated, and early initiation of peritoneal dialysis is preferred. This review discusses the most common causes, effects, and management of neurodevelopmental delays. Interventions in the preoperative, perioperative, and postoperative stages are examined, and the research indicates that preoperative factors are most influential in determining patient status. Neuromotor and cognitive delays are considered to be the most common adverse effects pediatric patients face after cardiac surgery. Both the AKI and neurodevelopmental studies lack sufficient patient populations, and more findings are needed to validate best practice evidence.

Keywords: Acute kidney injury, AKI, neurodevelopment, neurodevelopmental defect, neurodevelopmental deficit, neuromotor, cognitive, brain, development, pediatric, neonatal, infant, children, complications, management, surgery, cardiac, heart surgery, open heart surgery, cardiopulmonary bypass, CPB, FGF23, fibroblast growth factor 23, serum cystatin C, serum creatinine, postoperative, ICU, CCU, CVICU, cycled lighting, fluid overload, growth impairment, preoperative, perioperative, white matter brain injury

Complications and Management in Pediatric Heart Surgery

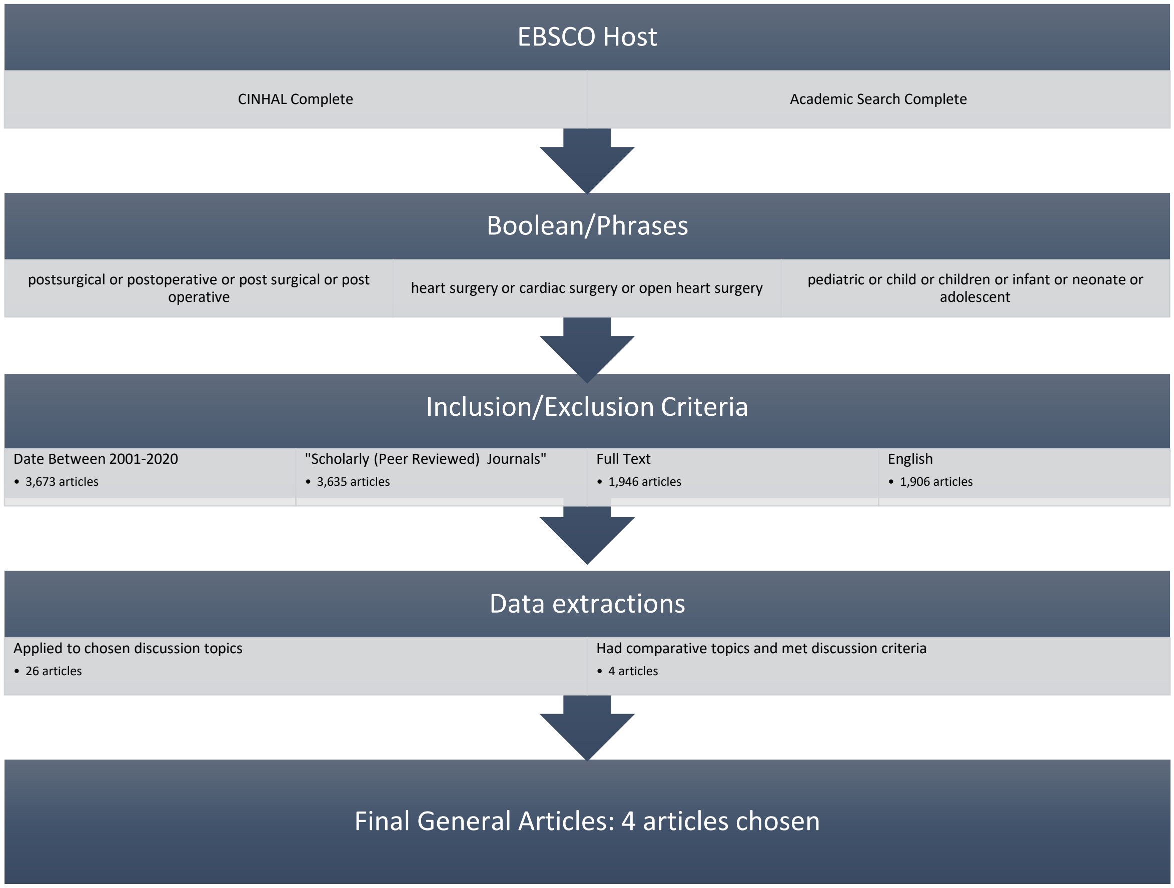
If someone were to try and list every postoperative complication a child could have after cardiac surgery, the list could go on forever. For every cardiac surgery, a pediatric patient is susceptible to an abundance of possible complications that increase morbidity and mortality (Brown et al., 2017). While most children after cardiac surgery are now able to survive longer into adulthood, the residual issues they face after their procedures and hospital stay may have long term negative effects (Ladak et al., 2019). Most complications are not single issues but are accompanied by several other problems. Due to the comorbidities that follow cardiac surgery, it is difficult to measure which specific complications result in a patient's increased morbidity and mortality (Agarwal, Wolfram, Saville, Donahue, & Bichell, 2013). Regardless of the exact cause, complications occur in 43% of cardiac patients, and the national benchmark of pediatric mortality after cardiac surgery is around 4% at most major institutions (Agarwal, Wolfram, Saville, Donahue, & Bichell, 2013). While measurements of each specific complication are not regularly reported, two complications that rank high in priority for a patient's morbidity are acute kidney injuries and negative neurological events (Brown et al., 2017). These negative outcomes are associated with longer intensive care unit (ICU) and hospital stays, increased mechanical ventilation times, and increased mortality (Agarwal, Wolfram, Saville, Donahue, & Bichell, 2013). Negative neurological and kidney events are serious complications that can result in long-term defects, and positive outcomes for these pediatric patients depends on quality multidisciplinary care (Agarwal, Wolfram, Saville, Donahue, & Bichell, 2013). This literature review is constructed to provide best practice procedures for preventing, treating, and managing acute kidney injury (AKI) and neurodevelopmental defects after pediatric cardiac surgery.

Methods

To determine current evidence regarding the diagnosis, management, and care of cardiovascular pediatric patients, EBSCO Host was utilized to find relevant literature as well as CINHAL and Academic Search Complete. CINHAL is a comprehensive source for nursing and nursing related literature, while Academic Search Complete is a general research database that contains scholarly journals. This literature review contains information on pediatric postoperative statistics, acute kidney injury, and neurodevelopment; for that reason, three different searches were needed to best locate relevant literature. The general search contained the Boolean Search Phrases: "postsurgical or postoperative or post surgical or post operative," and "heart surgery or cardiac surgery or open heart surgery," and "pediatric or child or children or infant or neonate or adolescent." For the inclusion/exclusion criteria, the date was set between 2001-2020, selected scholarly (peer reviewed) journals, selected full text only articles, and narrowed the search to only articles in English. This was the standard inclusion/exclusion criteria for each search. Next, article titles and abstracts were analyzed to select papers that would most helpful or pertinent in a literature review. From the chosen articles, their content determined if they met the criteria for discussion topics, and if the articles contained comparative or contrasting topics. In the end, four articles were selected to use in my final literature review for the general topics and discussions.

Figure 1

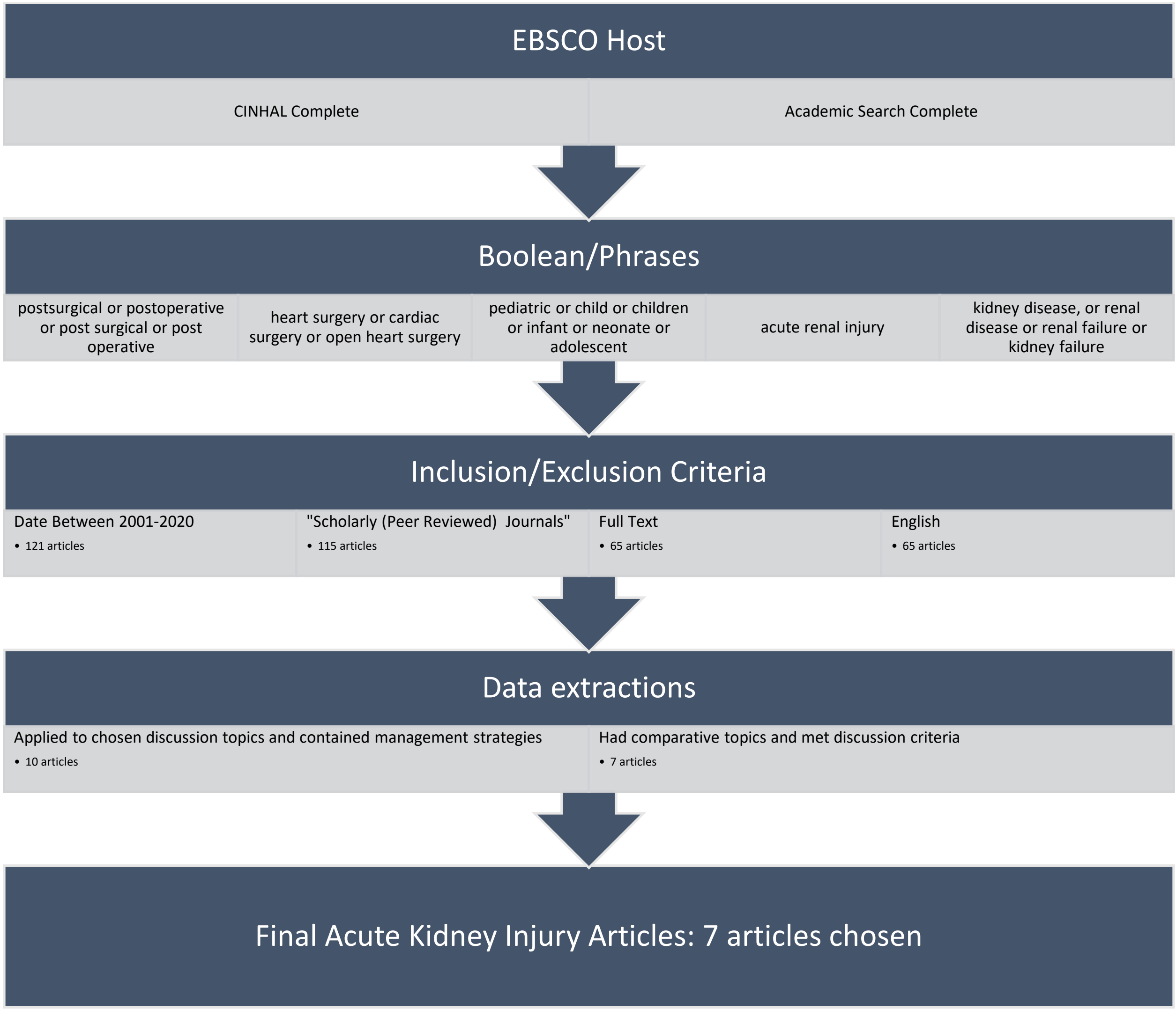
Flowchart for Finding General Topic Articles



Searching for articles related to acute kidney injury (AKI) and neurodevelopment followed similar search strategies. For both topics, CINHAL and Academic Search Complete were utilized. For acute kidney injury, the Boolean search phrases: “postsurgical or postoperative or post surgical or post operative,” and “heart surgery or cardiac surgery or open heart surgery,” and “pediatric or child or children or infant or neonate or adolescent,” and “acute renal injury,” and “kidney disease or renal disease or renal failure or kidney failure” were selected. The standard inclusion/exclusion criteria were used. For AKI, articles were chosen off their content and medical recommendations. Ten possible studies were preferred. After analyzing which papers could be used in a comprehensive review, seven articles met the criteria.

Figure 2

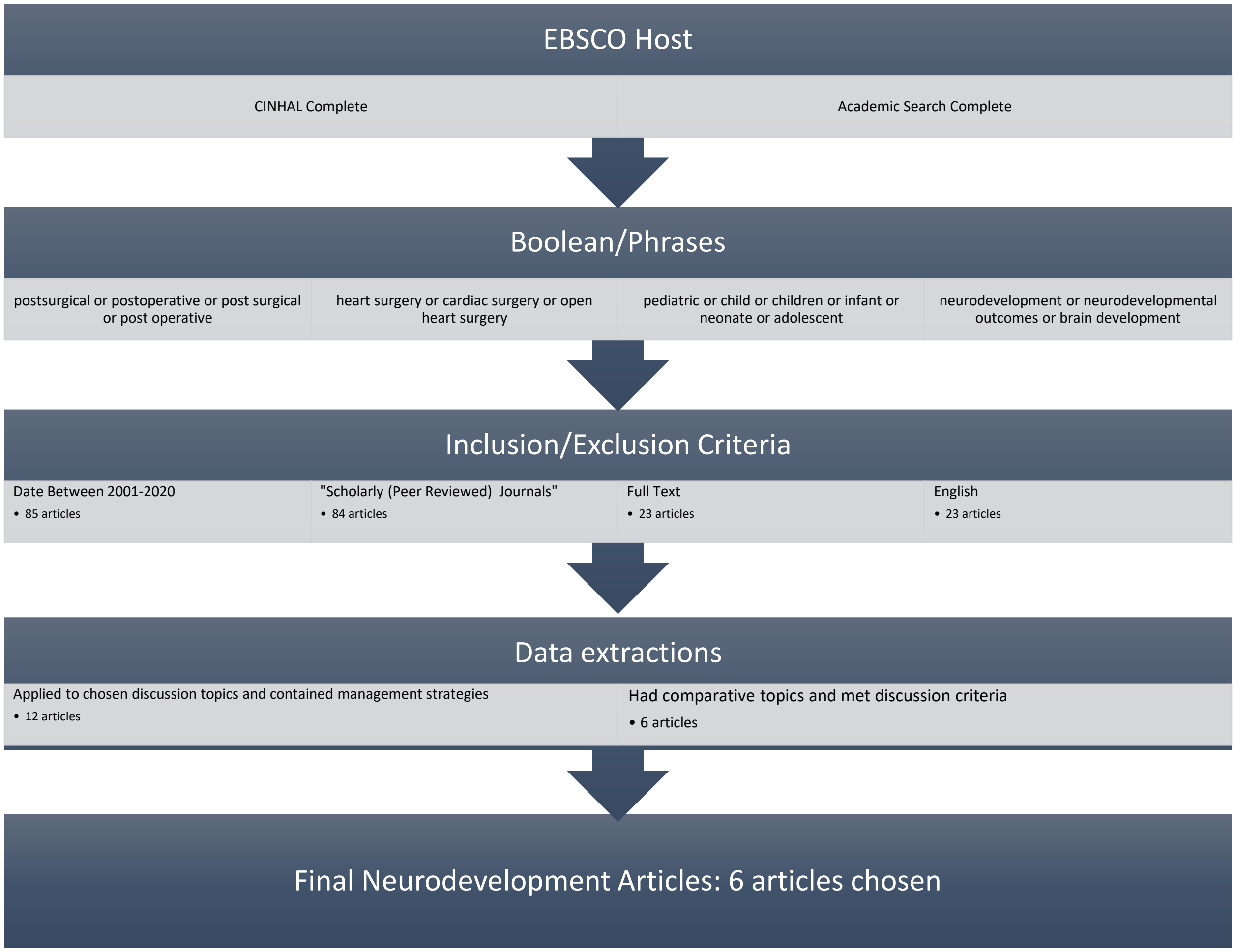
Flowchart for Finding Acute Kidney Injury Articles



The only difference in the search between AKI and neurodevelopment were the Boolean search phrases. To locate relevant neurodevelopment articles, the search phrases were: “postsurgical or postoperative or post surgical or post operative,” and “heart surgery or cardiac surgery or open heart surgery,” and “pediatric or child or children or infant or neonate or adolescent,” and “neurodevelopment or neurodevelopmental outcomes or brain development.” All other search criteria were the same as AKI’s search strategies, and after analysis, six articles were chosen for the literature review of neurodevelopment. In total, seventeen articles were evaluated for the literature review on managing pediatric heart surgery.

Figure 3

Flowchart for Finding Neurodevelopment Articles



Acute Kidney Injury

Arguably one of the most complex adverse effects of pediatric heart surgery is acute kidney injury (AKI). AKI is claimed to affect 20-60% of the pediatric cardiac postoperative population (Volovelsky et al., 2018). While this statistic differs slightly between the articles, it is important to note that a sizable percentage of pediatric patients develop AKI after their cardiac surgeries. The complexity of AKI stems from the fragility of the kidneys and is worsened by the lack of direct treatments or cures for AKI in the pediatric population. It is also not fully known how the pediatric and neonatal populations' kidneys adapt to major hemodynamic changes

(Kwiatkowski & Krawczeski, 2017). Management of symptoms and prevention is paramount, and early diagnosis is key to favorable outcomes. This section will discuss several articles about the pediatric population's association with kidney injuries and their suggestions regarding diagnosis, prevention, and management of AKI.

Causes of Acute Kidney Injury

In order to determine how to stop the development of AKI and correctly manage the severity when it occurs, clinicians need to look at the causes of kidney injury after cardiac surgery. While AKI is not caused by one specific factor, several studies have determined many strong sources of kidney injury. AKI is multifactorial and has many pathophysiological causes: renal ischemia, reperfusion injury, a maladaptive inflammatory response, oxidative stress, microemboli, alteration in tubule cell metabolism, direct tissue and endothelial injury, and cardiopulmonary bypass (CPB) are some direct causes of AKI (Kwiatkowski & Krawczeski, 2017). Zhang and Zhang (2018) contribute other factors to the causes of AKI: extracorporeal circulation, postoperative hypertension, endotoxins and free myoglobin, hemolysis, severe sepsis, acute heart failure, and a history of renal disease. Zheng, Xiao, Yao, and Han (2013) state claim more complex cardiac surgical procedures, a longer CPB duration, and a longer aortic clamping time (ACT) also contribute to AKI. Most of the factors on this extensive list of AKI causes are unplanned or nonmodifiable. The medical team cannot determine how every patient is going to react to the surgery and treatments, but they can look at the risk factors beforehand.

Risk Factors for Acute Kidney Injury

Risk factors for AKI can be a mix of modifiable and nonmodifiable, but knowing the risks beforehand helps medical teams prepare for possible complications and plan interventions. Kwiatkowski & Krawczeski (2017) state that the risks for AKI are younger age, higher surgical complexity, longer CPB time (especially greater than 180 min), preop ventilation, and using deep hypothermic circulatory arrest. Intraoperative hypertension, being on gentamicin pre-surgery, taking NSAIDs, and having low cardiac output syndrome are also factors that the authors claim worsen to postoperative outcomes. All of these risk factors correlate with having a more critical patient after surgery. This article also brings to light the possibility of selected gene variations either protecting or predisposing patients to AKI. Kwiatkowski and Krawczeski (2017) also claim there are some evidence of gene variations based off certain patients developing AKI and some not under the same backgrounds and circumstances, but they did not expand on this topic enough to make an accurate debate. All of the articles generally agree on what the causes and risk factors for AKI are, but the diagnoses differ.

Diagnosis of Acute Kidney Injury

While diagnosis of AKI varies based on hospital policy, traditional methods rely on serum creatinine. Due to many hospitals' reliance on serum creatinine, diagnosis of AKI is usually delayed. Both Kwiatkowski and Krawczeski (2017) and Zheng, Xiao, Yao, and Han (2013) emphasize that serum creatinine is not an early indicator of decreased renal function because serum creatinine levels do not increase until 50% of kidney function is lost. The authors also discovered that the increase in serum creatinine is usually seen around 24-48 hours after surgery; consequently, valuable time passes before any intervention is suggested. Soohoo et al. (2018) suggests that it might be easier to correct for fluid overload if using serum creatinine, rather than changing the whole diagnosis method. Fluid correction is recalculating the serum creatinine after taking account for the increased body water. The authors emphasize how important fluid correction is, because neonates have an increased percentage of body water, so increased fluid can dilute the increase of serum creatinine and mask an AKI diagnosis.

Zheng, Xiao, Yao, and Han (2013) looked to serum Cystatin C (CysC) as a diagnostic factor. The authors recognized a deficit in using serum creatinine as a diagnostic test and wanted to see if serum cystatin C was superior to clinical risk factors in the pediatric population. They determined that serum CysC concentrations were not significantly superior at predicting AKI after CPB than clinical risk factors. On the contrary, Kwiatkowski and Krawczeski (2017) state that serum cystatin-C is a biomarker that can be used to diagnose AKI sooner than serum creatinine. From the authors' viewpoint, serum CysC is more sensitive and specific in diagnosing AKI than creatinine levels. While the results of these two articles differ, both used particularly small patient populations to test their hypotheses (Zheng, Xiao, Yao, & Han, 2013), (Kwiatkowski & Krawczeski, 2017). This flaw shows that neither finding is ready for clinical practice; however, more studies need to be done before serum CysC is dismissed.

When considering biomarkers for AKI diagnosis, Volovelsky et al. (2018) studied fibroblast growth factor 23 (FGF23) before and after pediatric cardiac surgery to determine its role in AKI development. FGF23 is a biomarker that is associated with kidney function (Volovelsky et al., 2018). The authors tested FGF23 levels before and after operations and determined that FGF23 may have the potential to improve management of AKI without looking at clinical risk factors. They measured the FGF23 levels before surgery to assess the risk of AKI postoperatively. Research determined preoperative serum FGF23 was elevated in subjects who developed AKI. Preoperative levels in those who developed AKI were an average of 819 RU/mL, while the average FGF23 levels in those who did not develop AKI were 324.3 RU/mL. Preoperative levels of estimated GFR, serum phosphorus, and 25 hydroxyvitamin D did not differ between those who developed AKI and those who did not (Volovelsky et al., 2018). Volovelsky et al. also tested FGF23 levels postoperatively. They found that these concentrations rose 4-8 hours after cardiac surgery and were higher 12-24 hours after surgery in patients who developed AKI. This time frame is more appealing than serum creatinine, which takes 24-48 hours after surgery to increase (Kwiatkowski & Krawczeski, 2017). It is important to note that the FDA currently has no approved biomarker tests for AKI in the pediatric population (Kwiatkowski & Krawczeski, 2017). While looking at clinical risk factors is still important, Volovelsky et al.'s study may provide an extra layer of support in managing and predicting AKI after cardiac surgery.

While most conventional AKI management relies on preventing fluid overload, avoiding nephrotoxic medications, and initiating renal replacement therapy (RRT), Volovelsky et al.'s study relied on FGF23 levels. Their research is currently the largest prospective study done in the pediatric population to assess an AKI biomarker. There are currently no preoperative tests or biomarkers used in AKI management, so FGF23 levels show great potential. The authors showed that high pre-operative FGF23 levels helped predict AKI in children after heart surgery, as did a spike in FGF23 levels after surgery. They tested 83 children with congenital heart disease (CHD) who underwent CPB (Volovelsky et al., 2018). This study was a single-center study with a relatively low sample size, but 83 children were a relatively high sample size compared to much of the research available. One flaw in this study is that iron deficiency is associated with increased levels of FGF23. Also, when the authors added CPB time to the model in the study, the increased FGF23 levels after surgery did not retain statistical significance (Volovelsky et al., 2018). These considerations indicate that larger studies are needed in order to fully determine the validity of serum FGF23 levels.

Effects of Acute Kidney Injury

After the development of AKI, patients are more susceptible to poor outcomes. So much emphasis is placed on prevention and management because research has shown that even minor degrees of AKI correlate with worse clinical outcomes (Kwiatkowski & Krawczeski, 2017). Soohoo et al. (2018) talks about the negative effects that come with the development of AKI. AKI is an independent risk factor for increased duration of mechanical ventilation, longer ICU and hospital stays, and increased mortality (Soohoo et al., 2018). Kwiatkowski and Krawczeski (2017) advocate that AKI is a stronger predictor of death than having a single ventricle physiology or mechanical circulation support. Kwiatkowski and Krawczeski (2017) articulate that children who go on to develop AKI after surgery are at a higher risk of growth impairment, cardiac related rehospitalizations, and increased healthcare utilization 2-4 years postoperatively, even with all other controlled factors. The authors also show that patients with AKI have persistent elevation of kidney injury biomarkers for up to seven years postoperatively (Kwiatkowski & Krawczeski, 2017). This emphasizes that negative effects carry on even after the patient is discharged.

While effects of AKI can last after discharge, an important factor in considering in-hospital morbidity and mortality of postoperative pediatric cardiac patients is infection. Sepsis is the leading cause of death in patients with AKI (Soohoo et al., 2018). Soohoo et al. (2018) stresses that fluid corrected AKI was independently associated with the development of postoperative infections. The authors claim that AKI is an immunosuppressed state that increases the risk of infection. While AKI increases postoperative complications, having a postoperative infection also increases the duration of mechanical ventilation and hospital and ICU stays (Soohoo et al., 2018). Soohoo et al. also emphasizes that having AKI and a postoperative infection greatly increases the risk of negative outcomes. Therefore, preventing infections after cardiac surgery is even more important than originally thought, because AKI can worsen the immune state of postoperative patients.

Management of Acute Kidney Injury

Acute kidney injury is difficult to manage because there is no direct cure for AKI – prevention is key. Kwiatkowski and Krawczeski's (2017) management suggestions focus primarily around improving outcomes and treating and preventing fluid overload. AKI's outcomes worsen in relation to increased systemic fluid, so managing fluid overload is the primary focus. This study's outcome showed that the degree of fluid overload correlated with mortality: patients with less than 10% overload had a 30% mortality rate, while patients with greater than 20% overload died during their admission (Kwiatkowski & Krawczeski, 2017). This research shows how much impact is placed on preventing fluid overload and how imperative it is to do so. Kwiatkowski and Krawczeski (2017) recommend restricting fluids, using diuretics, giving renal vasodilators, and initiating early renal replacement therapy (RRT). The downside is restricting fluids can be difficult with the amount of infusions needed; diuretics and other medications may not improve AKI, or sometimes can even worsen it (Kwiatkowski & Krawczeski, 2017). Regarding RRT, the authors highlight that children with AKI who receive RRT only have a decreased mortality rate if peritoneal dialysis (PD) is used early. If it is initiated early, children were less likely to have fluid overload, had a decreased mechanical ventilation time, a decreased ICU stay, and no increase in expenditure (Kwiatkowski & Krawczeski, 2017). Zheng, Xiao, Yao, and Han (2013) are in congruence with Kwiatkowski and Krawczeski (2017) and emphasize that RRT can prevent the development of AKI only if initiated early. Kwiatkowski and Krawczeski (2017) were concerned that initiating PD for too long could potentially harm the kidneys even more. They studied the outcome of patients with longer PD and found that there is no evidence of further tubular injury if PD is prolonged. Both authors agree, regardless of the modality of RRT – intermittent hemodialysis and continuous venovenous hemofiltration are also acceptable methods – early initiation is paramount.

When it comes to preventing fluid overload, all the articles stand by RRT as paramount for prevention. While they all agree that RRT is necessary for the best outcome, most articles do not specify the method of RRT. For example, Kwiatkowski and Krawczeski (2017) discuss the importance of RRT, but do not specify a strong need to use PD over other RRT methods. Zhang, Jin, Zhang, Li, and Wu (2018) studied what RRT method was best and determined that using PD as RRT in the pediatric population after cardiac surgery was best to correct for fluid overload. They studied PD in the pediatric population and determined that the use of a single lumen central vein catheter as modified PD was a safe, feasible, and less invasive method for treating acute renal failure (ARF) in infants after cardiac surgery. The authors state that PD improved acidosis, hyperkalemia, hypoxemia, and low cardiac output. RRT with PD is preferred for infants and is a simple and low-cost method for treating volume overload and oliguria or anuria (Zhang, Jin, Zhang, Li, & Wu, 2018). All the patients in their study who used modified PD were restored to normal renal function. While the study achieved a high success rate, it was comprised of a small patient pool. Due to their small study size, the authors emphasize that PD should be used carefully in infants – especially newborns with acute renal failure (ARF) – because more studies need to be done.

The Need for New Management of Acute Kidney Injury

The downside of literature involving the pediatric population is limited studies for analysis, and much of the research data is comprised of an insignificant amount of patient observation data for pediatrics. Not only the small sample size, but there are little manipulations with methods because the pediatric population is extremely vulnerable. This means that studies usually only involve observing outcomes retrospectively or testing certain levels without interfering with the current treatment. Kwiatkowski and Krawczeski's (2017) study was the most extensive article found regarding AKI because it compiled research from many small studies. Even though advancements with AKI are small and discovered over long periods of time, the quickly advancing field will discover new treatments as more studies are publicized.

Acute kidney injury is arguably one of the most common adverse effects following cardiac surgery and cardiopulmonary bypass in the pediatric population. Much of the current research emphasizes preventing and managing AKI before it worsens, but there are some differences between the articles regarding diagnosis and management. Diagnosis methods require further studies with larger patient populations, but current research is headed in a positive direction. Relying on old methods and serum creatinine alone is no longer seen as the most useful prediction of AKI; researchers are working towards finding more accurate and swifter diagnoses. While management methods to prevent AKI seem to remain centered around preventing fluid overload, more research is suggesting initiating RRT before a high degree of fluid overload is suspected. As the outcomes of patients after cardiac surgery improve every year with new advancements, it is only fitting that our methods of diagnosis and management update in correlation with the growing surgical complexity.

Neurodevelopmental Deficits

As medical advancements continue to increase the life expectancies of children after heart surgery, the medical community is shifting its focus to improving quality of life. The most common and significant complication following survivors of pediatric heart surgery is neurodevelopmental disability (Gunn et al., 2016), which impacts performance and quality of life for patients years after their operations. Children with congenital heart disease (CHD) face many problems with cognitive and neuromotor function. Many issues facing patients with neurodevelopmental deficiencies after cardiac surgery are the lack of continuing support and resources as they age. Survivors of pediatric heart surgery are more likely to need remedial services – like tutoring and special education – as well as speech, physical, and occupational therapy (Gaynor et al., 2015). Because many cases of neurodevelopmental deficits after cardiac surgery are difficult to screen, patients are less likely to receive support (Ryan et al., 2019). In 2019, the Annual Pediatric Intensive Care Society had their 14th annual meeting. The main focus of this conference was to improve patient stress in the ICU/CCU and standardize long-term neurodevelopmental follow-up and support (Ryan et al., 2019). This initiative is a first step in aiding patients after their hospital leave. As an ICU staff, the focus on patient care relies heavily around perioperative and postoperative support. A shift in looking at innate and preoperative factors can help determine needed support for patients after surgery. The focus of this section is to analyze the effects cardiac surgery has on neurodevelopment, identify possible causes of damage during the preoperative, perioperative, and postoperative phases, and recognize potential modifications in the ICU to prevent neurodevelopmental issues.

Effects of Congenital Heart Disease and Surgery on Neurodevelopment

Children with CHD are an extremely vulnerable population. Their vulnerability is exacerbated by hemodynamic fluctuations, respiratory problems, major cardiac surgery, cardiopulmonary bypass, brain injury, and postoperative circulatory complications (Claessens et al., 2018). Cardiac surgery paired with a preexisting condition like CHD can cause many defects. These children face cognitive impairments, language difficulties, impulsivity and hyperactivity (Ryan et al., 2019), along with challenges in visual perception, executive functioning, and fine and gross motor skills (Gunn et al., 2016). Survivors of cardiac surgery as infants are more likely than the general population to need remedial services such as tutoring, special education, physical therapy, occupational therapy, and speech therapy (Gaynor et al., 2015). A social problem some survivors face is their deficits may be mild, but they often occur across multiple domains. This lack of perceived severity makes getting support in school and life difficult for these patients, as they usually do not qualify for remedial services (Ryan et al., 2019). Both Claessens et al. (2018) and Gaynor et al. (2015) discuss brain injury in CHD patients. They noted that many pediatric patients with CHD who required cardiac surgery show evidence of white matter brain injury (WMI) both before and after surgery (Claessens et al., 2018). Not only did these patients have smaller brain volumes at years two and six compared to their healthy peers (Gaynor et al., 2015), they also scored more than ten points lower on their IQ test (Claessens et al., 2018). While brain injury can occur before surgery even begins, affected children with added injury are behind the curve before their life even starts. The effects of CHD and corrective surgery extend far beyond the hospital, and anything the ICU staff can do to screen for or prevent these complications is paramount.

Preoperative Factors and Neurodevelopment

Looking to preoperative risk factors surrounding adverse neurodevelopmental outcomes give the medical team an idea of each patient’s increased risks. Claessens et al. (2018) brings to light that having CHD in itself is an immense risk factor for adverse neurodevelopmental effects. Slower brain growth and delayed maturation are caused by the decreased oxygen and nutrient delivery associated with CHD (Claessens et al., 2018). The effects of decreased circulation often leads to neurobehavioral deficits, which are usually present in a majority of patients before surgery even begins (Gessler, Schmitt, Prètre, & Latal, 2009). Gessler, Schmitt, Prètre, and Latal

(2009) emphasize that a large number of patients experience neuromotor abnormalities as a result of their cyanotic heart defect, which further impairs their later postoperative outcome. While the medical team cannot usually prevent the development of neurogenic deficits before surgery, they can use a patient's preoperative neurological impairments and risk factors to predict their postoperative outcomes (Gessler, Schmitt, Prètre, & Latal, 2009).

As technology and surgical interventions improve, the range of patient abnormalities that can be treated has increased. This has allowed patients with more serious heart conditions and greater surgical complexities to survive (Gaynor et al., 2015). This increased survival comes with the hazard of developing further neurological insufficiencies. Gaynor et al. (2015) suggests that improved outcomes of patients with a higher cardiac class are impeded by the greater risk of adverse neurodevelopmental outcomes. Patients with a higher cardiac class have a more serious heart disease, which hinders survival and quality of life (Gaynor et al., 2015). Gaynor et al. (2015) proved that patients who underwent more complex surgeries were also those who later scored lower on a psychomotor developmental scale. This shows that the cardiac class itself is a nonmodifiable risk factor that affects neuromotor performance (Gaynor et al., 2015). While the cardiac class and surgical complexity are things that cannot be controlled for, clinicians look to other preoperative risks that impact postoperative outcomes. These risk factors give the medical team a gauge of how severe the neurodevelopmental outcomes will be for each patient.

Claessens et al. (2018) studied the white brain matter injury of patients before and after cardiac surgery. They found that a large number of children showed evidence of moderate to severe white matter injury (WMI) on their preoperative MRI (Claessens et al., 2018). This confirms Gessler, Schmitt, Prètre, and Latal's (2009) statement that neurodevelopmental impairment usually exists before surgery. Claessens et al. (2018) then went on to study the postoperative MRIs and found that the children with moderate to severe preoperative WMI showed new moderate to severe WMI after their surgery. Clinicians can use these studies to take extra caution to prevent brain injury during surgery for patients who already show evidence of brain injury, as it will worsen with necessary interventions.

Another study done by Gaynor et al. (2015) identified specific risk factors for reduced mental and psychomotor outcomes. In Gaynor et al.'s (2015) study, they tested patients' Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) scores after cardiac surgery as part of the Bayley Scales of Infant and Toddler Development. The PDI scale tests control of gross muscle function, such as crawling and walking, and fine muscle skills, such as precise coordination and hand movements. The MDI assesses memory, numbers, problem solving, generalizing, vocalizing, language, and social skills (Gaynor et al., 2015). The authors found that, overall, patients scored lower on the PDI scales than the MDI scales after cardiac surgery, but the risk factors for lower scores varied for each scale. Lower MDI scores were found in patients who had a lower birth weight, were male, had less maternal education, or had a confirmed or suspected extracardiac or genetic anomaly (Gaynor et al., 2015). Those who scored lower on the PDI scale had a lower birth weight, were Caucasian, or had a confirmed or suspected extracardiac or genetic anomaly (Gaynor et al., 2015). PDI scores were also influenced by the cardiac class of the patient – those with a more serious heart disease had significantly lower PDI scores, but not lower MDI scores (Gaynor et al., 2015). Interestingly, this study discovered that gestational age, prenatal diagnosis, and neonatal status were not significantly associated with PDI or MDI scores. This is contrary to Gunn et al.'s (2016) study, which states that preoperative risk factors for neurological impairment were lower gestational age and smaller head circumference at birth. While some risk factors may differ, it is important for the medical team to know which elements influence postoperative outcomes. Even if the risks are nonmodifiable, being able to screen and prepare for them can influence the protective interventions and potentially improve neurological outcomes.

While medical teams hope for preoperative modifiable risk factors they can manipulate to improve their patients' outcomes, the vulnerable pediatric population does not have that luxury when it comes to cardiac surgery. Gaynor et al.'s (2015) study points to the idea that preoperative adverse neurodevelopmental outcomes were greatly influenced by innate patient factors rather than surgical management. The preoperative nonmodifiable risk factors of race, gender, birth weight, genetic anomalies, category of CHD, and maternal education were more important in determining postoperative outcomes than modifiable management factors (Gaynor et al., 2015). This means that more emphasis needs to be placed on preoperative risk screenings for patients before undergoing surgery in order to predict what interventions will be needed during and after surgery. Most mediations given to cardiac patients are done perioperatively and postoperatively (Ryan et al., 2019), but do the perioperative interventions actually influence later neurodevelopmental outcomes? Looking to the perioperative stage can give another indication of a patient's potential neurodevelopmental outcome.

Perioperative Factors and Neurodevelopment

When thinking of the greatest impact on neurodevelopment, surgery itself comes to mind. This popular view that surgery has the most control on the patient's neurological status may not be the case. As previously discussed in the preoperative section, CHD itself is a risk factor for neurodevelopmental deficits (Claessens et al., 2018). Gaynor et al. (2015) highlights the vulnerability of CHD patients during surgery. The authors state that CHD patients have a greater risk of brain injury due to hypoxia and ischemia, because CHD increases susceptibility to perioperative hemodynamic instability (Gaynor et al., 2015). The International Cardiac Collaborative on Neurodevelopment Investigators [ICCON] (2016) took Gaynor et al.'s (2015) hypotheses further by examining how operative factors affect the patients' PDI and MDI scores. They found that a longer support time using CPB was associated with lower PDI and MDI scores (ICCON, 2016). Gessler et al. (2009) agrees with CPB being a great influence and adds that the aortic clamp time during surgery may be another factor. Gessler et al. (2009) explains why CPB may be influential for neurodevelopmental status, stating that CPB invokes the systemic inflammatory response system, which is an inflammatory chain reaction that can trigger encephalopathy or brain dysfunction. While the pathophysiology behind cerebral injury is not fully understood, CPB may not be the only factor.

Gessler et al. (2009) brings to light that genetic abnormalities, the type of congenital heart defect, thromboembolic injuries, and perioperative inflammatory responses may all contribute to the type and severity of cerebral injury. Both Gessler et al. (2009) and The ICCON (2016) are in agreeance that innate patient factors and preoperative events may be more influential to neurodevelopmental status than CPB and surgery. The ICCON's (2016) findings that indicate longer CPB times affect MDI and PDI scores may be a surrogate for greater surgical complexity. Longer CPB time usually indicates a more complex surgery and patient status – leading to a patient who has a lower chance of a successful and non-problematic surgery. In the preoperative section, Gaynor et al. (2015) found that innate patient factors, such as higher cardiac class or preexisting neurogenic issues, are more predictive of postoperative patient status than previously thought. Gaynor et al.'s (2015) study explains The ICCON's (2016) hypothesis, stating that a more complex surgical case leads to a patient with a higher chance of negative neurodevelopmental outcomes.

While surgical techniques and operative status have an important role in a patient's neurodevelopmental status, innate patient and preoperative factors are more influential to a patient's neurodevelopmental outcome (ICCON, 2016). The events during surgery can help the medical team predict a patient's mortality, but neurodevelopmental insufficiencies are more accurately predicted by preoperative and inherent patient factors (ICCON, 2016). This does not mean surgery has no effect on patient status, but that more protective interventions need to be in place for patients with a higher congenital complexity. The medical team can use this knowledge to predict what patients will have more deficits based on their existing conditions and plan appropriate and individualized perioperative interventions.

Postoperative Factors and Neurodevelopment

As discussed in previous sections, CPB and support time are important factors in determining neurodevelopmental delays. The postoperative state is no different – support time and type affect neurodevelopmental status (Gessler et al., 2009). The ICCON (2016) measured the Psychomotor Developmental Index (PDI) and Mental Developmental Index (MDI) in their study and found that certain postoperative events lowered PDI and MDI scores. A patient who had a longer hospital stay, who used ECMO or VAD support after surgery, or had clinical seizures had lower PDI and MDI scores (ICCON, 2016). A patient who needed CPR after surgery had a lower PDI, but not MDI score (ICCON, 2016). These postoperative events cannot be avoided, but they show that every negative reaction a patient has lowers their future neurodevelopmental status.

Pediatric patients are transferred to a PICU, CVICU, or CCU after cardiac surgery. The state of the patient upon arrival to the PICU and during the next 48 hours is an important indicator of their predicted neurodevelopmental status (Gunn et al., 2016). Gunn et al. (2016)

identified several factors associated with impaired 2-year outcomes in pediatric patients. Metabolic acidosis on arrival to the PICU, a high lactate level 24 hours postoperatively, a prolonged PICU and hospital stay, and a delayed EEG recovery beyond 48 hours all contributed to compromised 2-year outcomes (Gunn et al., 2016). Children with severe language impairment two years after surgery had a mean arterial pH of 7.34 when they arrived to the PICU, compared to a pH of 7.44 in children without language deficiency (Gunn et al., 2016). Gunn et al. (2016) also asserts that children who had severe cognitive delay at two years after surgery stayed in the hospital for an average of 65 days, while children with mild or no cognitive delay stayed an average of 28 days. Gunn et al.'s (2016) study stresses that postoperative serum lactate levels predict the risk of cerebral injury, neurodevelopmental impairment, and death. After two years, children with severe cognitive impairment had an initial lactate that was 3.2 mmol/L higher than children with mild or no cognitive damage (Gunn et al., 2016). This finding indicates that PICU staff need to make managing serum lactate and pH a priority to help prevent neurodevelopmental injuries.

Cardiopulmonary bypass (CPB) creates an inflammatory response that is measured by IL-6, IL-8, C-reactive protein, and neutrophil count after surgery (Gessler et al., 2009). These levels can measure the inflammatory response, and Gessler et al. (2009) found that all four of these markers were increased after CPB when compared to their preoperative levels. Gessler et al.'s (2009) study states that IL-6 and IL-8 were strongly increased three hours after CPB, while C-reactive protein and neutrophil cell counts were higher 24 hours after CPB. While all of these factors indicate inflammation, the authors found that an increased IL-6 three hours after CPB was the best indicator of decreased neuromotor performance compared to other levels. They found that neuromotor performance was most affected by the systemic inflammatory reaction, while cognitive performance was not affected by CPB (Gessler et al., 2009). Gessler et al. (2009) states that preoperative IQ scores were the only significant predictor of postoperative IQ. Gessler et al.'s (2009) study can be used by the medical team to measure postoperative serum lactate, IL-6, IL-8, C-reactive protein, and neutrophil levels, and predict what later neurodevelopmental interventions will be needed for patients based off the results.

Gessler at el. (2009) discovered that neuromotor performance was most affected by CPB. The significant predictors of decreased neuromotor function are an increased CPB time, an increased aortic clamp time, the presence of a cyanotic heart defect, and an increased plasma IL-6 three hours after surgery (Gessler et al., 2009). All of these factors accounted for 67.8% of the variance of the response in Gessler et al.'s (2009) final multiple regression model. While these factors impact neuromotor performance, they may be surrogates for thromboembolic complications (Gessler et al., 2009). Thromboembolic complications are related to neuromotor disabilities; and Gessler et al. (2009) emphasizes that CPB duration, aortic clamp time, and cyanotic heart defects are all associated with thromboembolic difficulties. While Gessler et al. (2009), Gunn et al. (2016), and The ICCON (2016) all contain overlapping causes for neurodevelopmental defects, most disabilities are associated with the type of congenital heart defect, the procedure, and any possible CPB complications (Gessler et al., 2009). The discussed causes of complications in this section serves as parameters to monitor for patients returning to the PICU after surgery. The pH, serum lactate, CPB time, and hospital length of stay can give the health team an idea of the potential neurodevelopmental damage and help prepare for possible future deficits.

Postoperative Environment

While postoperative status is an important determinant of future neurodevelopmental impairment, the health care team cannot easily control postoperative status. What the team can control is the environment the patients come to after their difficult surgeries. Infants and children undergoing heart surgery are already at their most vulnerable state and have minimal reserves to adapt to stress (Ryan et al., 2019). The ICU is filled with bright lights, loud noises from staff and machines, and interruptions for care. Ryan et al. (2019) studied the psychoneuroendocrine systems and maladaptive stress response of the pediatric population in a CVICU. The authors found many sources of stress, including infants being separated from their mothers, routine ICU care, cold temperatures, lack of sleep, and staff noise. This repeated stress may result in long-lasting and profound changes in the infant's central nervous system development – changing the psychoneuroendocrine systems and stress response (Ryan et al., 2019).

Most admissions to the CVICU for infants are immediately after birth, because the deficit is impeding the infant's ability to sustain life. Ryan et al. (2019) found that separation of infants from their mothers deregulates the behavioral and neurodevelopmental trajectory of the infants. Cold temperatures in the CVICU may lead to cold stress, which causes a cascade of systemic events that ends in metabolic acidosis (Ryan et al., 2019). The authors studied infants in a CVICU over four days and found that infants woke up over 100 times, and the majority of sleep was less than 30 minutes at a time. When looking at routine CVICU care, Ryan et al. (2019) noticed that scheduled care impacts sleep-wake states, self-regulation, and brain development. The routine care also impacted the perception of pain in infants. This means that infants perceived pain even when there was none (Ryan et al., 2019). The biggest source of noise stress in the CVICU was created by staff (Ryan et al., 2019). All of these environmental factors that contribute to infant stress in the CVICU can be modified.

To create the best environment that promotes healing and growth, the CVICU staff needs to modify the unit. They should promote maternal-infant attachment by allowing parental engagement and participation as much as possible. They can maintain low light during the day and cycled dark periods at night to promote infant sleep. This cycled lighting method has been shown to decrease infants' heart rates and respiratory rates, increase weight gain, and increase sleep times (Ryan et al., 2019). The CVICU should manage pain and use proper infant positioning to promote comfort and reduce the development of positional deformities (Ryan et al., 2019). According to Ryan et al. (2019), the proper infant position is: flexed extremities and midline alignment with hand-to-mouth opportunities. Warmers, blankets, incubators, and hats should be given to avoid cold stress. Most importantly, the unit staff should create a group culture that keeps noise levels low by moving conversations away from patient rooms (Ryan et al., 2019). These environmental modifications can help improve patient outcomes by reducing stress and promoting sleep.

Quality Care Despite Negative Outcomes

Throughout the neurodevelopmental section, several articles have been analyzed regarding the cardiac preoperative, perioperative, and postoperative aspects of neurodevelopment. Motor abnormalities occur in 20-60% of pediatric patients (Gessler et al., 2009), and neurodevelopmental disabilities are the most common and damaging after cardiac operations (ICCON, 2016). Children with CHD are known to have frequent neurodevelopmental disabilities (Gessler et al., 2009), but only a low percentage of variance in early neurodevelopmental outcomes is explained by routine clinical variables (ICCON, 2016). Since studies have only identified a few modifiable risk factors to combat adverse neurodevelopmental outcomes, the medical community does not have much to work with (Gaynor et al., 2015).

Despite the lack of available modifications, researchers have continued to search for management strategies.

Gaynor et el. (2015) determined that patient and environmental factors, such as prematurity, genetic syndromes, and socioeconomic status, may be more important causes of adverse neurodevelopmental outcomes than operative approaches. Gessler et al. (2009) agreed with Gaynor et al. (2015) by stating that postoperative IQ was mostly influenced by the preoperative performance and IQ of the patient. Gessler et al. (2009) went on to say that neuromotor function was mostly influenced by the type of congenital heart defect, duration of CPB, aortic clamp time, and increased IL-6 from the systemic inflammatory reaction. While patient factors such as head circumference and gestational age predicted neurodevelopment, the patient’s immediate postoperative status in the PICU was the best predictor of mortality (Gunn et al., 2016). Even though neurodevelopment is most influenced by nonmodifiable factors, researchers still fight to discover what improvements the medical teams can make to positively impact their patients.

As a medical professional, there is always something more that can be done to help a patient. Ryan et al. (2019) emphasizes the need for standardization of long-term neurodevelopmental follow-up and support. The authors highlighted the variables the CVICU staff can control: noise levels, light exposure, pain management, proper positioning, and parental bonding and support (Ryan et al., 2019). These factors, along with policies and organizations that can improve long-term support and screening, can help improve the health and function of patients for years to come.

Searching for a Better Future

This literature review discussed the complications, management techniques, and outcomes of pediatric patients experiencing AKI or neurodevelopmental defects following cardiac surgery. After careful analysis of many scholarly articles, the amount of studies that find best practice interventions to prevent complications after cardiac surgery is inadequate. While the discussed articles provide excellent statistics, feedback, and management advice, more research is still needed. Cardiac complications affect 43% of patients, and better outcomes could lead to increased quality of life, decreased hospital stays, and increased morbidity and mortality (Agarwal, Wolfram, Saville, Donahue, & Bichell, 2013). Knowing that the health-related quality of life is decreased for pediatric cardiac patients (Ladak et al., 2019), it is imperative to continue to search for comprehensive interventions to improve outcomes and quality of life (Murni et al., 2019). With a high prevalence of patients experiencing acute kidney injury and neurodevelopmental defects, more prophylactic interventions should be considered for routine management of these complications. There needs to be an increase in the number of patients studied, more institutions need to contribute to research, and best practice techniques should be analyzed and reported in order to increase the rate of finding quality postoperative interventions. In the future, there are hopes to see a shift in management methods and routine best practice interventions in order to decrease difficulties for this vulnerable population.

References

Agarwal, H. S., Wolfram, K. B., Saville, B. R., Donahue, B. S., & Bichell, D. P. (2013). Postoperative complications and association with outcomes in pediatric cardiac surgery.

The Journal of Thoracic and Cardiovascular Surgery, *148*(2), 609-616. http://dx.doi.org/10.1016/j.jtcvs.2013.10.031

Brown, K. L., Pagel, C., Brimmell, R., Bull, K., Davis, P., Franklin, R. C., ... Mclean, A. (2017). Definition of important early morbidities related to paediatric cardiac surgery. *Cardiology in the Young*, *27*, 747-756. http://dx.doi.org/10.1017/S1047951116001256

Carlo, W. F., Clark, S. T., Borasino, S., & Alten, J. A. (2017). Impact of contrast exposure from computed tomography angiography on acute kidney injury after neonatal cardiopulmonary bypass surgery. *Congenital Heart Disease*, *12*, 540-545. http://dx.doi.org/10.1111/chd.12482

Claessens, N. H., Algra, S. O., Ouwehand, T. L., Jansen, N. J., Schappin, R., Haas, F., ... Benders, M. J. (2018). Perioperative neonatal brain injury is associated with worse school-age neurodevelopment in children with critical congenital heart disease. *Developmental Medicine & Child Neurology*, *60*, 1052-1058. http://dx.doi.org/10.1111/dmcn.13747

Gaynor, W. J., Stopp, C., Wypij, D., Andropoulos, D. B., Atallah, J., Atz, A. M., ... Newburger, J. W. (2015). Neurodevelopmental outcomes after cardiac surgery in infancy. *American Academy of Pediatrics*, *135*, 816-825. http://dx.doi.org/10.1542/peds.2014-3825

Gessler, P., Schmitt, B., Prètre, R., & Latal, B. (2009). Inflammatory response and neurodevelopmental outcome after open-heart surgery in children. *Pediatr Cardiol*, *30*, 301-305. http://dx.doi.org/10.1007/s00246-008-9354-5

Gunn, J. K., Beca, J., Hunt, R. W., Goldsworthy, M., Brizard, C. P., Finucane, K., ... Shekerdemian, L. S. (2016). Perioperative risk factors for impaired neurodevelopment after cardiac surgery in early infancy. *Arch Dis Child*, *101*, 1010-1016. http://dx.doi.org/10.1136/archdischild-2015-309449

Hirano, D., Ito, A., Yamada, A., Kakegawa, D., Miwa, S., Umeda, C., ... Ida, H. (2017). Independent risk factors and 2-year outcomes of acute kidney injury after surgery for congenital heart disease. *American Journal of Nephrology*, *46*, 204-209. http://dx.doi.org/10.1159/000480358

Kwiatkowski, D. M., & Krawczeski, C. D. (2017). Acute kidney injury and fluid overload in infants and children after cardiac surgery. *Pediatric Nephrology*, *32*, 1509-1517. http://dx.doi.org/10.1007/s00467-017-3643-2

Ladak, L. A., Hasan, B. S., Gullick, J., Awais, K., Abdullah, A., & Gallagher, R. (2019). Health-related quality of life in surgical children and adolescents with congenital heart disease compared with their age-matched healthy sibling: a cross- sectional study from a lower middle-income country, Pakistan. *Arch Dis Child*, *104*, 419-425. http://dx.doi.org/10.1136/archdischild-2018-315594

Murni, I. K., Djer, M. M., Yanuarso, P. B., Putra, S. T., Advani, N., Rachmat, J., ... Sukardi, R. (2019). Outcome of pediatric cardiac surgery and predictors of major complication in a developing country. *Annals of Pediatric Cardiology*, *12*, 38-44. http://dx.doi.org/10.4103/apc.APC_146_17

Ryan, K. R., Jones, M. B., Allen, K. Y., Marino, B. S., Casey, F., Wernovsky, G., & Lisanti, A. (2019). Neurodevelopmental outcomes among children with congenital heart disease: At-risk populations and modifiable risk factors. *World Journal for Pediatric and Congenital Heart Surgery*, *10(6)*, 750-758. http://dx.doi.org/10.1177/2150135119878702

Soohoo, M., Griffin, B., Jovanovich, A., Soranno, D. E., Mack, E., Patel, S. S., ... Gist, K. M. (2018). Acute kidney injury is associated with subsequent infection in neonates after the Norwood procedure: a retrospective chart review. *Pediatric Nephrology*, *33*, 1235-1242. https://doi.org/10.1007/s00467-018-3907-5

The International Cardiac Collaborative on Neurodevelopment Investigators. (2016). Impact of operative and postoperative factors on neurodevelopmental outcomes after cardiac operations. *The Annals of Thoracic Surgery*, *102*, 843-849. https://doi.org/10.1016/j.athoracsur.2016.05.081

Volovelsky, O., Terrell, T. C., Swain, H., Bennett, M. R., Cooper, D. S., & Goldstein, S. L. (2018). Pre-operative level of FGF23 predicts severe acute kidney injury after heart surgery in children. *Pediatric Nephrology*, *33*, 2363-2370. https://doi.org/10.1007/s00467-018-4024-1

Zhang, L., Jin, Y., Zhang, F., Li, H., & Wu, Q. (2018). Modified peritoneal dialysis for treatment of acute renal failure after complex congenital heart surgery in infants. *The Heart Surgery Forum*, *21*(4), 286-289. http://dx.doi.org/10.1532/hsf.1915

Zheng, J., Xiao, Y., Yao, Y., & Han, L. (2013). Is serum cystatin C an early predictor for acute kidney injury following cardiopulmonary bypass surgery in infants and young children? *Kaohsiung Journal of Medical Sciences*, *29*, 494-499. http://dx.doi.org/10.1016/j.kjms.2013.01.004

Appendix A

Pediatric Cardiac Surgery Research Articles

Author(s) & Date	**Research Method**	**Findings Relevant to Scope and Magnitude of Health Issue, Health Behavior, Population, etc.**
Agarwal, H. S., Wolfram, K. B., Saville, B. R., Donahue, B. S., & Bichell, D. P (2013)	Quantitative Research	This study determined that postoperative surgical complications occur in 43% of pediatric CHD patients. The national benchmark for overall mortality after CHD surgery is <4% at most institutions. They discussed how pediatric cardiac surgeries are inconsistently reported, and that postoperative cardiac and extracardiac complications affect mortality, hospital stay, cost, and quality of life. The authors also emphasized the need of accurate recognition of complications, relevant treatments, and standardized treatment outcomes.
Brown, K. L., Pagel, C., Brimmell, R., Bull, K., Davis, P., Franklin, R. C., ... Mclean, A. (2017)	Mixed Methods Research (both quantitative and qualitative)	The authors discussed the morbidities and mortalities affecting pediatric patients after cardiac surgery and discussed its impact on the patients and hospital. They found that children who have longer hospital stays after cardiac surgery developed higher levels of neurological disabilities.
Carlo, W. F., Clark, S. T., Borasino, S., & Alten, J. A. (2017)	Quantitative Research	The authors determined that having a computed tomography angiography as part of CHD interventions did not affect postoperative risk of AKI.
Claessens, N. H., Algra, S. O., Ouwehand, T. L., Jansen, N. J., Schappin, R., Haas, F., ... Benders, M. J. (2018)	Mixed Methods Research (both quantitative and qualitative)	The authors studied neonatal brain white matter injury (WMI) before and after cardiac surgeries. They also looked at how patients’ IQs were affected by surgery. They determined that children who underwent cardiac surgery and showed evidence of WMI had smaller brain volumes, lower average IQ’s, more attention problems, and an increase in motor difficulties than children without WMI. Children with WMI and CHD showed worse outcomes compared to children who only had WMI and did not have CHD, proving that the combination of having CHD and WMI worsens neurodevelopmental outcomes.
Gaynor, W. J., Stopp, C., Wypij, D., Andropoulos, D. B., Atallah, J., Atz, A. M., ... Newburger, J. W. (2015)	Mixed Methods Research (both quantitative and qualitative)	The authors measured both psychomotor developmental index (PDI) and mental development index (MDI) on children after cardiac surgery, with an emphasis on how preoperative factors influence scores. They determined that risk factors for lower PDI and MDI scores had some differences. Certain adverse events after cardiac surgery negatively impacts either PDI, MDI, or both; while some factors do not impact either PDI or MDI scores.

		Both PDI and MDI scores improved over time, but cardiac surgery altered brain development in the majority of subjects. They also highlighted that more patients are facing adverse neurodevelopmental outcomes due to increasing survival rates after surgery.
Gessler, P., Schmitt, B., Prètre, R., & Latal, B. (2009)	Mixed Methods Research (both quantitative and qualitative)	The authors discussed how CPB affects brain function after cardiac surgery. They determined that postoperative IQ was most influenced by preoperative neuro performance and was worsened by increasing surgical complexity. They discussed how neurodevelopmental disabilities are frequent in children with CHD, and often exist before surgery. They also analyzed how inflammatory mediators (IL-6 and IL-8) affected neuromotor performance.
Gunn, J. K., Beca, J., Hunt, R. W., Goldsworthy, M., Brizard, C. P., Finucane, K., ... Shekerdemian, L. S. (2016)	Quantitative Research	This study discussed preoperative risk factors for worse postoperative outcomes after cardiac surgery. The authors determined that postoperative factors like metabolic acidosis in the PICU, higher lactate levels 24 hours after surgery, prolonged PICU stay, and a delayed EEG recovery beyond 48 hours all led to cognitive impairment. Cognitive and language performance were most severely and frequently affected after pediatric cardiac surgery.
Hirano, D., Ito, A., Yamada, A., Kakegawa, D., Miwa, S., Umeda, C., ... Ida, H. (2017)	Quantitative Research	This study shows that survival rates for pediatric patients after cardiac surgery is lower if they had AKI. The authors identified that CPB, higher surgical complexity, and elevated serum creatinine were factors that led to increased mortality. They suggested the medical team anticipate renal risk and initiate renal protective interventions before and after surgery.
Kwiatkowski, D. M., & Krawczeski, C. D. (2017)	Mixed Methods Research (both quantitative and qualitative)	The authors describe how AKI is common in infants and children after cardiac surgery, and how AKI is associated with worse outcomes and an increased mortality. They Emphasized that serum creatinine is not a reliable diagnostic factor and recommend prophylactically initiating peritoneal dialysis to prevent fluid overload.
Ladak, L. A., Hasan, B. S., Gullick, J., Awais, K., Abdullah, A., & Gallagher, R. (2019)	Mixed Methods Research (both quantitative and qualitative)	This is the first study that explores both general and health related quality of life (HRQOL) and its associations in children after cardiac surgery. The authors found that children with CHD who underwent cardiac surgery had lower general and HRQOL compared to healthy age-matched siblings. They emphasized the need to standardize HRQOL assessments in CHD patients.

Murni, I. K., Djer, M. M., Yanuarso, P. B., Putra, S. T., Advani, N., Rachmat, J., ... Sukardi, R. (2019)	Quantitative Research	This study found that one-fifth of children who underwent cardiac surgery experienced one or more major complications, with a mortality rate around 13%. The authors emphasized a need for comprehensive interventions that reduce mortality, decrease complications, and improve quality of life for pediatric patients following cardiac surgery. They suggest decreasing and preventing the occurrence of clinical factors that result in a longer CPB, increased blood lactate, and higher inotropes.
Ryan, K. R., Jones, M. B., Allen, K. Y., Marino, B. S., Casey, F., Wernovsky, G., & Lisanti, A. (2019)	Mixed Methods Research (both quantitative and qualitative)	The authors discussed and measured the factors that negatively influence patients' neurodevelopmental outcomes, such as environment, stress, and fragility. They suggested ways to improve ICU environment, minimize stress, decrease pain, and protect brain development in pediatric patients after cardiac surgery.
Soohoo, M., Griffin, B., Jovanovich, A., Soranno, D. E., Mack, E., Patel, S. S., ... Gist, K. M. (2018)	Mixed Methods Research (both quantitative and qualitative)	This study analyzed the relationship between AKI and sepsis/postoperative infections, and the authors determined that AKI is an immunosuppressed state. They also discussed the downsides of serum creatinine as a diagnostic factor, and recommended correcting for fluid overload before measuring serum creatinine.
The International Cardiac Collaborative on Neurodevelopment Investigators (2016)	Mixed Methods Research (both quantitative and qualitative)	This is the follow up study of Gaynor et al. (2015). The authors measured both psychomotor developmental index (PDI) and mental development index (MDI) on children after cardiac surgery but focused on how intraoperative and postoperative factors influence scores. They determined that intraoperative and postoperative factors only accounted for 5% of the variances in PDI and MDI scores. They also determined that greater surgical complexity is the common denominating factor that influences patients' neurodevelopmental outcome.
Volovelsky, O., Terrell, T. C., Swain, H., Bennett, M. R., Cooper, D. S., & Goldstein, S. L. (2018)	Mixed Methods Research (both quantitative and qualitative)	This study measured FGF23 levels both before and after cardiac surgery and determined that higher FGF23 levels led to an increased development of AKI and an increased morbidity and mortality. Elevated FGF23 levels before surgery was associated with an increased development of AKI. Elevated FGF23 levels after surgery was associated with a higher development of AKI and morbidity and mortality.

Zhang, L., Jin, Y., Zhang, F., Li, H., & Wu, Q. (2018)	Mixed Methods Research (both quantitative and qualitative)	This study analyzed the risk factors for development of AKI after cardiac surgery. The authors determined that peritoneal dialysis (PD) is the best method of renal replacement therapy and helps improve patient outcomes. PD improves acidosis, hyperkalemia, hypoxemia, and low cardiac output – which increase postoperative conditions.
Zheng, J., Xiao, Y., Yao, Y., & Han, L. (2013)	Mixed Methods Research (both quantitative and qualitative)	The authors tested if serum cystatin C could help diagnose AKI before clinical risk factors and conventional tests. They determined that serum cystatin C was not superior at detecting AKI after surgery compared to clinical risk factors (such as higher surgical complexity, longer aortic clamping time, and longer cardiopulmonary bypass).

Appendix B

AKI – acute kidney injury

ARF – acute respiratory failure

Academic Search Complete – Database on EBSCO host

CCU – Cardiac Care Unit

CHD – congenital heart disease

CINHAL – Cumulative Index of Nursing and Allied Health Literature, Database on EBSCO host

CPB – cardiopulmonary bypass

CVICU – Cardiovascular Intensive Care Unit

EBSCO Host – Main database used to collect research articles from sub-databases, like CINHAL and Academic Search Complete

FDA – Food and Drug Administration

FGF23 – fibroblast growth factor 23

GFR – glomerular filtration rate

ICU – Intensive Care Unit

MDI – Mental Developmental Index

MRI – magnetic resonance imaging

NSAIDs – nonsteroidal anti-inflammatory drugs

PD – peritoneal dialysis

PDI – Psychomotor Developmental Index

RRT – renal replacement therapy

WMI – white matter injury