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REVIEW PAPER

From Other Journals: A Review of Recent Articles by Our Editorial Team

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Abstract
In this review we provide a brief description of recently published articles addressing topics relevant to pediatric cardiologists. Our hope is to provide a summary of the latest articles published recently in other journals in our field. The articles address (1) The impact of COVID-19 in individuals with congenital heart disease through the life span. Patients with a genetic syndrome and adults at advanced physiological stage were at highest risk for moderate/severe infection. (2) Echocardiographic findings of the multisystem inflammatory syndrome in children showing a high prevalence of myocardial injury and systolic dysfunction that improves in the subacute phase. (3) A score assessment of the Fontan associated liver disease which correlated with the risk for Fontan failure. (4) Grown-up congenital heart surgery in 1093 consecutive cases showed that the 30 day mortality may underestimate the mortaility and that the 6 months mortality is likely a better measure in this population. (5) Cone versus conventional repair for Ebstein's anomaly showed better midterm results and freedom from tricuspid regurgitation after the cone operation. (6) Association between race/ethnicity, illness severity, and mortality in children undergoing cardiac surgery. The study showed that the African American race associated with increased disease severity and thus higher postoperative mortality compared to the caucausian race.

Keywords Fontan · COVID-19 · Liver disease · Fontan association liver disease · The multisystem inflammatory syndrome in children · GUCH · Ebstein's anomaly · Cone repair · Race/ethnicity disparity

The Impact of Coronavirus Disease 2019 (COVID-19) on Patients with Congenital Heart Disease Across the Lifespan: The Experience of an Academic Congenital Heart Disease Center in New York City [1]

This study assessed the impact and predictors of Coronavirus Disease 2019 (COVID-19) infection and severity in a cohort of congenital heart disease (CHD) patients at a large CHD center in New York City.

The team at Columbia University performed a retrospective review of all individuals with CHD followed at their center who were diagnosed with COVID-19 between 3/1/2020 and 7/1/2020. The study used a primary endpoint of moderate/severe response to COVID-19 infection defined as (a) death; or (2) need for hospitalization and/or respiratory support. Over the 4 months study period, there were 53 COVID-19 positive patients with CHD median age 34 years, 10 (19%) were < 18 years old and 52 were symptomatic. 31 (58%) had complex congenital anatomy including 10 (19%) with a Fontan repair. Eight patients (15%) had a genetic syndrome including 5 (9%) with Trisomy 21, 2 (4%) with DiGeorge syndrome and 1 (2%) with VACTERL association. Six patients (11%) had pulmonary hypertension (PH), and nine (17%) were obese. Among adults, 18 (41%) were physiologic class C or D. For the entire cohort, nine (17%) had a moderate/severe infection, including three deaths (6%). Both patients living in long-term care facilities at the time of infection died. Of note, six of the 7 hospitalized patients with moderate/severe infection had worsening hypoxemia requiring supplemental oxygen and 3 required intubation. One hospitalized patient required inotropic support. Two underwent transthoracic echocardiography during admission with no change from baseline. No changes in cardiac medications were required for patients with mild infections

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or those treated as an outpatient. After correcting for multiple comparisons, the presence of a genetic syndrome (OR 35.82: $P = 0.0002$), and in adults, physiological Stage C or D (OR 19.38: $P = 0.002$) were significantly associated with moderate/severe infection.

The study concluded that the number of symptomatic COVID-19 patients was relatively low. CHD patients with a genetic syndrome and adults at advanced physiological stage were at highest risk for moderate/severe infection. Thus despite evidence that adult-onset cardiovascular disease is a risk factor for worse outcomes among patients with COVID-19, patients with CHD without concomitant genetic syndrome, and adults who are not at advanced physiological stage, do not appear to be disproportionately impacted. The study included no patients with coronary artery disease and thus the impact of acquired heart disease on patients with CHD cannot be evaluated. It is our approach to recommend that our patients be cautious using social distancing, face mask and strictly follow the recommendation from public health organization during these unprecedented times.

Echocardiographic Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19 in the United States [2]

High number of children with a severe inflammatory syndrome in the setting of coronavirus disease 2019 are seen in the United States and Europe. This syndrome has been named the multisystem inflammatory syndrome in children (MIS-C) and this study aimed to analyze echocardiographic manifestations in MIS-C. The retrospective study included a total of 28 MIS-C, 20 healthy age-matched control subjects and 20 classic Kawasaki disease (KD) patients. The study reviewed echocardiographic parameters in the acute phase of the MIS-C and KD groups, and during the subacute period in the MIS-C group (interval 5.2 ± 3 days). Myocardial injury in MISC was defined as BNP > 500 pg/ml and troponin > 0.3 ng/ml. Only 1 case in the MIS-C group (4%) had coronary artery dilatation (z score = 3.15 in the right coronary artery) in the acute phase with resolution during early follow-up. No segmental aneurysms were detected.

Left ventricular (LV) systolic and diastolic function measured by deformation parameters were worse in patients with MIS-C compared with KD. Moreover, MIS-C patients with myocardial injury were more affected than those without myocardial injury in all functional parameters. The strongest parameters to predict myocardial injury in MIS-C were global longitudinal strain, global circumferential strain, peak left atrial strain, and peak longitudinal strain of right ventricular free wall. The preserved LV ejection fraction (EF) group in MIS-C showed diastolic dysfunction. During the subacute period, LVEF returned to normal (median from 54 to 64%; $P < 0.001$) but diastolic dysfunction persisted.

Unlike classic KD, coronary arteries are usually spared in early MIS-C; however, myocardial injury is more common. Even patients with preserved EF showed subtle changes in myocardial deformation, suggesting subclinical myocardial injury. During the short term follow-up, there was good recovery of systolic function but persistence of diastolic dysfunction and no coronary aneurysms. This elegant pilot study have used detailed echocardiography including ventricular and atrial strain to assess patients with MIS-C. There is a need for more long term data to inform the follow up protocols used in patients with MIS-C. Registries and collaboration between institutions will provide more detailed data to answer these remaining questions.

Evaluation of Fontan Failure by Classifying the Severity of Fontan-Associated Liver Disease: A Single-Center Cross-Sectional Study [3]

Fontan-associated liver disease (FALD) is increasingly common in adults with a Fontan circulation, but no general classification of FALD severity exists. Classifying the severity of FALD can be very helpful identifying patients at high risk for Fontan failure. In this study, the researchers proposed a scoring system to grade the severity of FALD and analyzed its applicability association with Fontan failure. The study included 129 successive Fontan patients received a comprehensive hepatic assessment from 2017 to 2019. The FALD score was based on results from laboratory testing, hepatic ultrasound and transient elastography by assigning scoring points for each abnormality detected. One scoring point was assigned for an increase of ALT, AST, γGT or bilirubin above the upper reference limit. Similarly, patients received 1 scoring point for a decrease of thrombocytes below the lower reference limit. Elastography values were graded and categorized using median and percentiles: patients with values ≤ 25th percentile were assigned 0 points, values from 25th to 50th percentile 1 point, values from 50th to 75th percentile 2 points and values ≥ 75th percentile 3 points. Hepatic ultrasound was analyzed based on detection of the most common hepatic abnormalities noted in Fontan patients. For score calculation, 1 point was assigned for each hepatic abnormality observed resulting in a maximum of 9 points in this category. Scoring points of all 3 diagnostic modalities were added to the final FALD score. The FALD score was categorized using median and percentiles: A score ≤ 3.0 scoring points (≤ 25th percentile) was graded as absent/mild, between 4.0 and 5.0 scoring points as moderate and ≥ 6.0 scoring points (≥ 75th percentile) as severe extent of FALD.

FALD was graded absent/ mild, moderate and severe in 53, 26 and 50 patients, respectively. Cardiopulmonary exercise capacity was significantly impaired in patients with severe FALD compared to patients with absent/mild FALD ($P=0.001$). The FALD score significantly correlated with pulmonary artery pressure ($P=0.001$), end-diastolic ventricular pressure ($P<0.001$), hepatic venous pressure ($P=0.004$) and wedged hepatic venous pressure ($P=0.009$). Fontan failure was present in 21 patients. FALD was graded moderate in 2 and severe in 19 of these patients. The FALD score accurately discriminated patients with and without Fontan failure (sensitivity 90.5%, specificity 71.3%). The FALD score significantly correlates with impaired Fontan hemodynamics. A cut-off value > _6.0 has a high diagnostic accuracy in detecting Fontan failure.

Grown-Up Congenital Heart Surgery in 1093 Consecutive Cases: A "Hidden" Burden of Early Outcome [4]

Grown-ups with congenital heart disease (GUCH) are defined as aged 16 years and older in the United Kingdom. This population is increasing as more and more infants with congenital heart disease survive into adulthood [5]. The barriers to GUCH surgical patients are variable and the usual risk models either do not apply or are not validated for this population. Moreover, the effects of age related comorbidities can further complicate the medical situation, increasing the surgical risk that is usually accompanied by complex anatomy, reoperations and technical challendges. The authors postulated that even though 30 day postoperative mortality is low, it may not reflect adequate adverse outcome monitoring [6]. They aimed to study whether intensive care unit (ICU) stay ≥ 7 days and 6 month mortality were better predictors of adverse event.

A total of 1026 patients were studied at Middlesex and the Heart Hospital who underwent 1093 consecutive cardiac surgeries. Congenital heart disease diagnostic complexity was assessed according to the 32nd Bethesda Conference of the American College of Cardiology and procedure complexity via Aristotle Basic Complexity (ABC) Score. In addition, the cohort was divided into 4 time eras for quality assurance. During the study period, 30-day mortality improved significantly, with an overall 30-day mortality of 1.5% ($n=16$) and a 6- month mortality of 2.4% ($n=26$). In the 26 patients who died within 6 months, cardiorespiratory arrest was the most common cause in 15 (57.7%) patients. Other causes were multiorgan failure in 3, heart failure in 2, and 1 death each of hypoxic brain damage, bronchopneumonia, aortic aneurysm dissection, retroperitoneal hemorrhage, intracranial bleeding, and sepsis. Complete follow up was obtained in 99.8% of patients and median follow up after discharge was 5.2 years (IQR 1.8–9.4 years). Estimated survival rates at 1,5 and 10 years were 97.0%, 93.8%, and 91.8%, respectively. A total of 60 patients (5.5%) had prolonged ICU stay.

Predictors of adverse outcome were New York Heart Association class III or higher, preoperative renal failure, disease of great complexity, preoperative ventilator support, cardiopulmonary bypass time, and concomitant procedures. Interestingly, the 6 month mortality was remarkably lower during the contemporary era despite stable ABC scores while the number of patients with prolonged ICU stay increased. The authors concluded, with the current era of low 30 day mortality, extended 6 month mortality and prolonged ICU stay may be more realistic measures of adverse outcome.

Cone Versus Conventional Repair for Ebstein's Anomaly [7]

Ebstein's anomaly is a rare anomaly of the tricuspid valve (TV) that accounts for 1% of all congenital heart diseases [8]. Original TV reconstruction techniques for Ebstein's anomaly were based on ventricular plication, with the aim to bridge leaflet gaps and to decrease the massively dilated tricuspid annulus. Dr. da Silva and colleagues [9] developed the cone technique in 1993 that has since been adopoted by centers performing a large number of these surgical procedures. This study was designed to look at TV function after conventional versus cone repair for Ebstein's anomaly.

Patients who underwent TV surgery between 1985 and 2018 were included with few exclusions: TV surgery at another institution, neonatal surgery, congenitally corrected transposition of the great arteries. Tricusid regurgitation (TR) was graded as none, trivial, mild, moderate, or severe according to the echocardiographer. Patients were categorized into three groups: cone repair, other repair techniques and valve replacement.

A total of 218 patients underwent Ebstein's repair during the study period, and 151 were included. Thirty-nine patients underwent cone repair, 107 patients underwent other repair techniques, and 5 patients underwent valve replacement. The operative mortality was 1.3% ($n=2$). Failed valve repair (defined as in-hospital death, conversion to replacement, or in-hospital reoperation) was less frequent after cone repair than after other repair techniques (5%, $n=2$ vs 20%, $n=21$, $P=0.039$). Mean follow-up was 12.3 years (cone repair: 3.7 years). The 5-year cumulative incidence of moderate or greater recurrent tricuspid regurgitation was lower after cone repair than after other repair techniques (8% vs 32%, $P=0.03$). Among the patients undergoing other repair techniques, the 15-year cumulative incidence of moderate or greater recurrent tricuspid regurgitation, severe tricuspid

regurgitation, and reoperation was 58%, 37%, and 31%, respectively. During follow-up, 18 patients died (13 of cardiac and 5 of noncardiac causes). Among patients who died of cardiac causes, 10 of 13 had all 3 characteristics—moderate or greater tricuspid regurgitation, atrial fibrillation, and New York Heart Association classification III and IV—at their last medical evaluation.

Recurrent and progressive TR is frequently seen after conventional repair of Ebstein's anomaly. In addition, 20% of the patients required conversion to TV replacement or redo operations before hospital discharge. The recently introduced cone repair yielded consistent tricuspid function over an 8-year follow-up period. Although long-term results after the cone procedure are still pending, the authors concluded that the cone repair should be the primary treatment for patients with Ebstein's anomaly as mid-term results are encouraging.

Association Between Race/Ethnicity, Illness Severity, and Mortality in Children Undergoing Cardiac Surgery [10]

Earlier studies have demonstrated an association between minority race/ethnicity and higher mortality after cardiac surgery in both adult and pediatric populations [11]. However, the influence of illness severity on racial/ethnic disparities in congenital cardiac surgical outcomes has not been fully studied. Delineating the association between race/ethnicity, severity of illness, and cardiac surgical outcomes is vital in appropriately allocating resources to reduce identified disparities. With this study, the authors examined the asoscition between race/ethnicity and severity of illness in children undergoing congenital heart surgery in a multi-institutional registry of critically ill children.

Children younger than 18 years old undergoing cardiac surgery admitted to the intensive care unit ($n = 40{,}545$) between 2009 and 2016 from the Virtual Pediatric Systems (VPS, LLC, Los Angeles, Calif) database were studied. This database is a clinical registry of 154 pediatric ICUs in North America. Multivariate logistic regression analysis was conducted to evaluate the association between race/ethnicity and mortality, separating the analysis by preoperative and postoperative admission status. Pediatric Index of Mortality 2 (PIM 2), Pediatric Risk of Mortality 3 (PRISM 3) and Pediatric Index of Cardiac Surgical Intensive Care Mortality (PICSIM) scores were examined as a mediator between race/ethnicity and mortality. Of the 154 units, 111 reported race/ethnicity for > 85% of their respective patients. There was significant variation across all race/ethnicity groups for gender, age, prematurity, number of chronic conditions, STAT category, and severity of illness scores.

Younger age, prematurity, increasing number of chronic conditions, increasing surgical complexity, and postoperative admission status were associated with greater severity of illness for all or most of the 3 measures (PIM 2, PRISM 3, and PICSIM). African-American patients had statistically significant higher severity of illness scores when compared with their white counterparts. In multivariate models of intensive care unit mortality after adjustment, African-American patients had a higher odds of postoperative mortality (OR 1.40, 95% CI 1.04–1.89) when compared with white children. This increased odds of mortality was mediated through higher severity of illness, because adjustment for severity of illness removed this survival disadvantage for black patients.

This survival disparity is eliminated after accounting for severity of illness, suggesting that increased severity of illness may be an important driver of health disparities for children undergoing congenital heart surgery. Research focusing on disparities during the preoperative and intraoperative period may help further elucidate the etiologies behind surgical survival disparities (Table 1).

Table 1 Summary of the six studies in this review

Author	Study summary
Lewis et al.	*The Impact of Coronavirus disease 2019 (COVID-19) on Patients with Congenital Heart Disease* Retrospective study of all patients with CHD at Columbia University with COVID19 53 patients, 52 symptomatic and median age 34 while 10 are < 18 years 31 with complex CHD including 10 Fontan. 9 required hospitalization. 3 Death The presence of a genetic syndrome (OR 35.82), and in adults, physiological Stage C or D (OR 19.38) were significantly associated with moderate/severe infection CHD patients with a genetic syndrome and adults at advanced physiological stage were at highest risk for moderate/severe infection
Matsubara et al.	*Echo findings in multisystem inflammatory syndrome in children (MIS-C)* 28 pts with MIS-C, 20 healthy children and 20 patients with Kawasaki Only 1/28 (4%) had coronary ectasia of the right coronary that normalized with follow up MIS-C patients also had worse LV systolic and diastolic function than the KD group (all strain parameters, $P < 0.05$) and cardiogenic shock was much more frequent (85 vs. 5% incidence) Follow up in 5 days showed normalization of systolic function but persistent diastolic dysfunction measures Systolic and diastolic function were both abnormal in the acute phase, while diastolic dysfunction, as measured by multiple strain parameters, was more likely to persist
Schleiger et al.	*Evaluation of Fontan failure by classifying the severity of Fontan-associated liver disease: a single-center cross-sectional study* 129 patients with Fontan received a comprehensive liver assessment The FALD score was based on results from laboratory testing, ultrasound and elastography FALD was graded absent/ mild, moderate and severe in 53, 26 and 50 patients, respectively FALD severity associated with Fontan failure and Fontan pressure The FALD score correlates with impaired Fontan haemodynamics and Fontan failure
Haapanen et al.	*Grown-up Congenital Heart Surgery in 1093 Consecutive Cases: A "Hidden" Burden of Early Outcome* 1093 cardiac surgeries were performed in 1026 GUCH patients 30-day mortality improved significantly, with an overall 30-day mortality of 1.5% 6-month mortality and prolonged ICU stay were 2.4% and 6.7%, respectively Predictors of adverse outcome were NYHA Class III or higher, preoperative renal failure, disease of great complexity, preoperative ventilator support, cardiopulmonary bypass time and concomitant procedures Extended 6-month mortality and prolonged ICU stay reporting may be more realistic measures of adverse outcomes for counseling GUCH patients at risk
Burri et al.	*Cone versus conventional repair for Ebstein's anomaly* 151 patients at a single center were studied Cone repair = 39 patients, other repair techniques = 107, valve replacement = 5 Failed valve repair was less frequent after cone repair than after other repair techniques (5% vs 20%, $P = 0.039$) 5-year cumulative incidence of moderate or greater recurrent tricuspid regurgitation was lower after cone repair (8% vs 32%, *P*-0.03) Cone repair provided a higher rate of successful repair and a lower incidence of moderate or greater recurrent tricuspid regurgitation at the midterm follow-up
Tjoeng et al.	*Association between race/ethnicity, illness severity, and mortality in children undergoing cardiac surgery* Virtual Pediatric database was studied involving 154 pediatric ICU African-American patients had statistically higher severity of illness scores African-American patients had higher odds of postoperative mortality Adjustment for severity of illness removed this survival disadvantage for black patients Although African-American children undergoing cardiac surgery had higher postoperative mortality, this survival difference appears to be mediated via severity of illness

CHD congenital heart disease, *GUCH* Grown-ups with congenital heart disease

Authors' Contributions The author summarized the recent published literature in this review.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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