Worse hospital outcomes for children and adults with COVID-19 and congenital heart disease

Danielle D. Strah, MD[a], Katie A. Kowalek, MD[b], Kevin Weinberger, DO[a], Jenny Mendelson, MD[b], Andrew W. Hoyer, MD[c], Scott E. Klewer, MD[c], Michael D. Seckeler MD, MSc[c]

Affiliations: [a]Department of Pediatrics, University of Arizona; [b]Department of Pediatrics (Critical Care), University of Arizona; [c]Department of Pediatrics (Cardiology), University of Arizona

Address correspondence to: Michael D. Seckeler, University of Arizona, Department of Pediatrics (Cardiology), 1501 N. Campbell Ave, PO Box 245073, Tucson AZ, 85724, mseckeler@peds.arizona.edu, 520-626-5585. orcid.org/0000-0001-9013-5723

Word count: 855

Declarations of Interest: None

Keywords: COVID-19, Congenital Heart Disease

Abstract

Objectives:

The aim of the current study is to investigate hospitalization outcomes of COVID-19 positive children and adults with moderate or severe congenital heart disease to children and adults without congenital heart disease.

Methods:

Retrospective review using the Vizient Clinical Data Base for admissions of patients with an ICD-10 code for COVID-19 from April 2020 – March 2021. Admissions with COVID-19 and with and without moderate or severe congenital heart disease (CHD) were stratified into pediatric (<18 years) and adult (≥18 years) and hospital outcomes were compared.

Results:

There were 9,478 pediatric COVID-19 admissions, 160 (1.7%) with CHD and 658,230 adult COVID-19 admissions, 389 (0.06%) with CHD. Pediatric admissions with COVID-19 and CHD were younger (1 vs 11 years), had longer length of stay (22 vs 6 days), higher complication rates (6.9 vs 1.1%), higher mortality rates (3.8, 0.8%) and higher costs ($54,619 vs 10,731; p <0.001 for all). Adult admissions with COVID-19 and CHD were younger (53 vs 64 years, p <0.001), had longer length of stay (12 vs 9 days, p <0.001), higher complication rates (8 vs 4.8%, p=0.003) and higher costs ($23,551 vs 13,311, p <0.001).

Conclusions:

This appears to be the first study to report the increased hospital morbidities and costs for patients with CHD affected by COVID-19. Our hope is that these findings will help counsel patients moving forward during the pandemic.

Worse hospital outcomes for children and adults with COVID-19 and congenital heart disease

As of July 2021, there were 183,696,230 cases of coronavirus disease 2019 (COVID-19) globally, with 3,975,227 deaths.[1] Patients who have underlying cardiovascular conditions such as hypertension and coronary heart disease have additional morbidity and mortality for COVID-19.[2, 3] Patients with moderate and severe congenital heart disease (CHD) have empirically been considered higher risk from COVID-19 [3, 4] though, due to their relatively small population, there are sparse data regarding the outcomes of hospitalized patients with moderate and severe CHD along with COVID-19. The purpose of this study was to use a national discharge database to analyze report hospital outcomes for COVID-19 in the setting of moderate and severe CHD compared to those without CHD.

Methods

The Vizient Clinical Data Base is an analytic platform for performance improvement populated by hundreds of health systems and community hospitals in the United States, including nearly all academic medical centers. The database includes demographics, mortality, length of stay (LOS), complications, readmission rates, resource utilization and other information. After approval from the University of Arizona Institutional Review Board, which waived the need for informed consent for this retrospective review of deidentified data, we queried the database for hospital discharge data from April 2020 – March 2021 for all admissions with an ICD-10 code for moderate or severe CHD, as defined by the 2018 Adult CHD guidelines (Table 1),[5] and the diagnostic code for COVID-19 (U07.1), which went into effect April 1, 2020. The Adult CHD guidelines determined CHD severity by native anatomy, surgical repair and current physiology.[4]

Diagnoses of an isolated atrial septal defect, congenital heart block, isolated levocardia, tortuous aortic arch, anomalous subclavian artery and any "NOS" cardiac diagnoses were excluded. The comparison group (No CHD) consisted of admissions with no ICD-10 codes for CHD and with the diagnostic code for COVID-19. The groups were further divided into pediatric (<18 years) and adult (≥18 years). Comparison of outcomes between acyanotic and cyanotic lesions was also performed. Demographics, LOS, rate of the presence of complications listed in the Vizient Clinical Data Base[6], in-hospital mortality and total hospital costs were collected. To determine if there was a difference in admission severity of illness or mortality risk between the groups, queries were preformed from Vizient-defined "Acuity Scale Mortality" (severity of illness at admission) and "Relative Expected Mortality" (mortality risk at admission. These were converted to dichotomous values or Low/normal (comparable or less risk) and High (above normal risk) for comparison. Continuous, normally distributed data are presented as mean ± standard deviation, non-normally distributed as median (interquartile range) and categorical data as number (%). Comparisons were made between groups using the *t*-test for normally distributed data, the Kruskal-Wallis test for non-normally distributed data and the χ^2 test for categorical data. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS 27 (IBM Corporation, Armonk, New York, USA).

Results

There were 9,478 total pediatric COVID-19 admissions, 160 (1.7%) with CHD, and 658,230 total adult COVID-19 admissions, 389 (0.06%) with CHD. Demographics and hospital outcomes are shown in Table 2. Pediatric admissions with COVID-19 and CHD were younger, had longer LOS, higher presence of complications listed in the Vizient Clinical Data Base,

higher mortality rates and higher costs (Table 2). There were no sex-based or race/ethnicity-based differences. Adult admissions with COVID-19 and CHD were younger, had longer LOS, higher presence of complications listed in the Vizient Clinical Data Base and higher costs (Table 2). There were no differences in in-hospital mortality rates or sex-based or race/ethnicity-based differences. The specific CHD diagnoses for the Pediatric and Adult groups are listed in Table 3. There were no differences in acute hospital outcomes (LOS, presence of complications listed in the Vizient Data Base or mortality) between cyanotic and acyanotic diagnoses (Table 4). Pediatric admissions with CHD had higher severity of illness and mortality risk at admission, but adults with CHD had lower severity of illness at admission with no difference in mortality risk (Table 5).

Discussion

COVID-19 is a rapidly evolving global pandemic. While non-congenital cardiovascular comorbidities have been identified as risk factors for poor outcomes,[2] to the best of our knowledge, ours is the first national study to demonstrate worse hospital outcomes for children and adults with moderate and severe CHD who are hospitalized for COVID-19.

While young age is thought to be protective from COVID-19 for the general population, our findings do not support this for children or adults with CHD. In addition, the longer LOS and higher costs for patients with CHD is consistent with their expected fragility due to their underlying cardiac diagnoses, which is also highlighted by the higher severity of illness and mortality risk in the Pediatric group. It is also interesting that the adults with CHD had lower severity of illness at admission, but a similar mortality risk. The higher costs may also be due to more aggressive treatment provided to this population. There may be reductions in severe

COVID-19 and hospitalizations with the introduction of vaccines against the SARS-CoV-2 virus, but this will not likely be available for young children for some time.

There are limitations to administrative database studies due to a lack of detail for some of the heart conditions and current functional status as well as potential errors in data entry. The code for COVID-19 (U07.1) is utilized for both symptomatic and asymptomatic individuals who have tested positive for the virus. However, it is unlikely that the current findings of worse outcomes in the CHD group were simply due to the group without CHD only having asymptomatic COVID-19 and the group with CHD only having symptomatic COVID-19. Despite these limitations, given the novelty of the COVID-19 pandemic and the relative rarity of moderate and severe CHD, using a large administrative database allows us to have a better sense of the current status of the COVID-19 pandemic than any single center study could provide.

The current study suggests worse hospital outcomes when patients with CHD are hospitalized for COVID-19 infection, including higher mortality for children. These data stress the importance of primary prevention with vaccination, social distancing and masking measures to reduce severe COVID-19 and hospitalizations and also to increase herd immunity to protect the children who are too young to receive the vaccines at this time. These findings can help to further guide treatment strategies and prioritize patients for vaccination.

Acknowledgements: None

Declarations: None of the authors have disclosures relevant to the current study

Funding: There is no funding for the current study

Conflicts of interest/Competing interests: Not applicable

Availability of data and material: Data not available

Code availability: N/A

Author Contributions DDS: Conceptualization, Methodology, Investigation, Writing-Original Draft. KAK: Conceptualization, Methodology, Writing-Review & Editing. KW: Conceptualization, Writing-Review & Editing. JM: Writing - Review & Editing. AWH: Writing - Review & Editing. SEK: Writing - Review & Editing. MDS: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing-Review & Editing, Supervision.

Compliance with Ethical Standards

Conflict of interest: Danielle D. Strah declares that she has no conflict of interest. Katie A. Kowalek declares that she has no conflict of interest. Kevin Weinberger declares that he has no conflict of interest. Jenny Mendelson: declares that she has no conflict of interest. Andrew W. Hoyer declares that he has no conflict of interest. Scott E. Klewer declares that he has no conflict of interest. Michael D. Seckeler declares that he has no conflict of interest.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent: The need for informed consent was waived for this study of deidentified data.

References

1. Dong E, Du H and Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. 2020;20:533-534.

2. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, Jain SS, Burkhoff D, Kumaraiah D, Rabbani L, Schwartz A and Uriel N. COVID-19 and Cardiovascular Disease. *Circulation*. 2020;141:1648-1655.

3. Alsaied T, Aboulhosn JA, Cotts TB, Daniels CJ, Etheridge SP, Feltes TF, Gurvitz MZ, Lewin MB, Oster ME and Saidi A. Coronavirus Disease 2019 (COVID-19) Pandemic Implications in Pediatric and Adult Congenital Heart Disease. *J Am Heart Assoc*. 2020;9:e017224.

4. Seckeler MD, Thomas ID, Andrews J, Meziab O, Moe T, Heller E and Klewer SE. Higher Cost of Hospitalizations for Non-cardiac Diagnoses in Adults with Congenital Heart Disease. *Pediatr Cardiol*. 2018;39:437-444.

5. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, Khairy P, Landzberg MJ, Saidi A, Valente AM and Van Hare GF. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139:e698-e800.

6. Haffner MR, Le HV, Saiz AM, Han G, Fine J, Wolinsky P and Klineberg EO. Postoperative In-Hospital Morbidity and Mortality of Patients With COVID-19 Infection Compared With Patients Without COVID-19 Infection. *JAMA Netw Open*. 2021;4:e215697.

Table 1 - ICD-10 codes for moderate and severe congenital heart disease, as defined by the 2018 Adult Congenital Heart Disease guidelines. DILV = double inlet left ventricle; HLHS = hypoplastic left heart syndrome; TA = tricuspid atresia.

Moderate congenital heart disease	**ICD-10 codes**
Partial or total anomalous pulmonary venous return	Q26.2, Q26.3, Q26.4
Anomalous left coronary artery from the pulmonary artery	Q24.5
Atrioventricular septal defect	Q21.2
Aortic stenosis (congenital)	Q23.0
Mitral stenosis (congenital)	Q23.2
Coarctation of the aorta	Q25.1, Q25.42
Cor triatriatum	Q24.2
Ebstein anomaly	Q22.5
Subpulmonary stenosis	Q24.3
Patent ductus arteriosus	Q21.4, Q25.0
Pulmonary regurgitation	Q22.2
Pulmonary stenosis	Q22.1
Peripheral pulmonary stenosis	Q25.6, Q25.7, Q25.71
Sinus of Valsalva fistula	Q25.4
Subaortic stenosis	Q24.4
Supravalvar aortic stenosis	Q25.3
Tetralogy of Fallot	Q21.3
Double aortic arch	Q25.45
Complex congenital heart disease	**ICD-10 codes**

Double outlet right ventricle	Q20.1
Interrupted aortic arch	Q25.21
Single ventricle (DILV, TA, HLHS, etc)	Q20.4, Q22.4, Q22.6, Q23.4, Q25.2, Q25.29, Q25.41
Pulmonary atresia	Q22.0, Q25.5
Transposition of the great arteries (d-, l- or congenitally corrected)	Q20.3, Q20.5
Truncus arteriosus	Q20.0
Criss cross heart, heterotaxy	Q20.6
Eisenmenger	I27.83
Double outlet left ventricle	Q20.2

Table 2 - Demographics and hospital outcomes for Pediatric (<18 years old) and Adult (≥18 years) admissions for COVID-19 infection with and without moderate or severe congenital heart disease (CHD). Data are presented as n (%), mean ± standard deviation or median (interquartile range). CHD = congenital heart disease; LOS = length of stay; No CHD = no congenital heart disease. Data from the Vizient Clinical Data Base used by permission of Vizient. All rights reserved.

Pediatric (<18 years)	**CHD (n = 160)**	**No CHD (n = 9,318)**	***p***
Age (y)	1 (0.2, 5)	11 (2, 15)	<0.001
Female (n, %)	77 (48)	4,770 (51)	0.442
Race/ethnicity (n, %)			
White	72 (45)	4,146 (45)	0.899
Black	40 (25)	2,054 (22)	
Hispanic	53 (33)	2,983 (32)	
Asian	3 (2)	223 (2)	
LOS (d)	22.2 ± 42.7	6.3 ± 20.6	<0.001
Complications (n, %)	11 (6.9)	101 (1.1)	<0.001
Death (n, %)	6 (3.8)	79 (0.8)	<0.001
Direct costs ($)	54,619 ± 124,413	10,731 ± 39,952	<0.001
Adult (≥18 years)	**CHD (n = 389)**	**No CHD (n = 657,841)**	***p***
Age (y)	53 (35, 65)	64 (50, 76)	<0.001
Female (n, %)	192 (49)	312,510 (48)	0.465

Race/ethnicity (n, %)			
White	236 (61)	364,706 (55)	0.121
Black	70 (18)	143,500 (22)	
Hispanic	69 (18)	127,274 (19)	
Asian	17 (4)	23,057 (4)	
LOS (d)	11.6 ± 14.5	8.7 ± 11.0	<0.001
Complications (n, %)	31 (8)	31,385 (4.8)	0.003
Death (n, %)	41 (10.5)	79,594 (12.1)	0.346
Direct costs ($)	23,551 ± 44,503	13,311 ± 25,891	<0.001

Table 3 - Congenital heart defect diagnoses for the Pediatric and Adult groups. Note, some admissions may have more than one cardiac diagnosis, so the total number of diagnoses exceeds the total for each group. DILV = double inlet left ventricle; HLHS = hypoplastic left heart syndrome; TA = tricuspid atresia. Data from the Vizient Clinical Data Base used by permission of Vizient. All rights reserved.

Moderate congenital heart disease	**Pediatric CHD** **n**	**Adult CHD** **n**
Partial or total anomalous pulmonary venous return	6	15
Anomalous left coronary artery from the pulmonary artery	9	89
Atrioventricular septal defect	11	14
Aortic stenosis (congenital)	1	14
Mitral stenosis (congenital)	1	6
Coarctation of the aorta	16	26
Cor triatriatum	0	5
Ebstein anomaly	6	16
Subpulmonary stenosis	1	2
Patent ductus arteriosus	61	34
Pulmonary regurgitation	1	5
Pulmonary stenosis	4	14
Peripheral pulmonary stenosis	27	34
Sinus of Valsalva fistula	0	0
Subaortic stenosis	2	13
Supravalvar aortic stenosis	0	2

Tetralogy of Fallot	22	31
Double aortic arch	1	4
Complex congenital heart disease		
Double outlet right ventricle	12	8
Interrupted aortic arch	2	0
Single ventricle (DILV, TA, HLHS, etc)	36	34
Pulmonary atresia	13	11
Transposition of the great arteries (d-, l- or congenitally corrected)	8	25
Truncus arteriosus	2	3
Criss cross heart, heterotaxy	3	2
Eisenmenger	0	0
Double outlet left ventricle	0	0

Table 4 - Hospital outcomes for Pediatric (<18 years old) and Adult (≥18 years) admissions for COVID-19 infection with cyanotic and acyanotic moderate or severe congenital heart disease. Data are presented as n (%) or mean ± standard deviation. LOS = length of stay. Note, some patients had multiple diagnoses. Data from the Vizient Clinical Data Base used by permission of Vizient. All rights reserved.

Pediatric (<18 years)	**Cyanotic (n = 109)**	**Acyanotic (n = 261)**	***p***
LOS (d)	28.0 ± 41.3	34.9 ± 57.0	0.253
Complications (n, %)	9 (8.3)	34 (13)	0.192
Death (n, %)	3 (2.8)	15 (5.7)	0.222
Adult (≥18 years)	**Cyanotic (n = 122)**	**Acyanotic (n = 388)**	***p***
LOS (d)	9.9 ± 11.3	12.6 ± 16.3	0.089
Complications (n, %)	10 (8.2)	33 (8.5)	0.916
Death (n, %)	13 (10.7)	34 (8.8)	0.528

Table 5 – Severity of illness at admission and mortality risk for Pediatric (<18 years) and Adult (≥18 years) admissions for COVID-19 infection with and without congenital heart disease. Data are presented as n, %. Data from the Vizient Clinical Data Base used by permission of Vizient. All rights reserved.

Pediatric (<18 years)	**CHD (n = 160)**	**No CHD (n = 9,318)**	***p***
Severity of Illness			
Low/normal (n, %)	128 (80)	8,982 (96.4)	<0.001
High (n, %)	32 (20)	336 (3.6)	
Mortality Risk			
Low/normal (n, %)	77 (48.1)	6,241 (67)	<0.001
High (n, %)	83 (51.9)	3,077 (33)	
Adult (>18 years)	**CHD (n=389)**	**No CHD (n=657,841)**	***p***
Severity of Illness			
Low/normal (n, %)	174 (44.7)	235,795 (35.8)	<0.001
High (n, %)	215 (55.3)	422,046 (64.2)	
Mortality Risk			
Low/normal (n, %)	307 (78.9)	526,085 (80)	0.605
High (n, %)	82 (21.1)	131,756 (20)	