The Coronavirus Disease 2019 Pandemic among Adult Congenital Heart Disease Patients: Findings of a One-year Multicentric, International Study of the EPOCH Collaboration

FJ. Ruperti Repilado1, M. Greutmann2, J. Bouchardy3, P. Brennan4, L. Campens5, P. Gallego6, R. Garcia-Orta7, AS. Jensen8, M. Ladouceur9, B. Miranda-Barrio10, M. Morissens11, J. Rueda Soriano12, AE. Van Den Bosch13, D. Tobler14, M. Schwerzmann1

*(1) Bern University Hospital, Inselspital, Bern, Switzerland (2) University Hospital Zurich, Cardiology, Zurich, Switzerland (3) University Hospital Centre Vaudois (CHUV), Cardiology, Lausanne, Switzerland (4) Belfast Health and Social Care Trust, Cardiology, Belfast, United Kingdom of Great Britain & Northern Ireland (5) Ghent University Hospital, Cardiology, Ghent, Belgium (6) UNIVERSITY HOSPITAL VIRGEN DEL ROCIO, Cardiology, Seville, Spain (7) University Hospital Virgen de las Nieves, Cardiology, Granada, Spain (8) Rigshospitalet - Copenhagen University Hospital, Cardiology, Copenhagen, Denmark (9) Hopital Europeen Georges Pompidou- University Paris Descartes, Cardiology, Paris, France (10) University Hospital Vall d'Hebron, Cardiology, Barcelona, Spain (11) Brugmann University Hospital, Cardiology, Brussels, Belgium (12) Hospital Universitario y Politecnico La Fe, Cardiology, Valencia, Spain (13) Erasmus University Medical Centre, Cardiology, Rotterdam, Netherlands (The) (14) University Hospital Basel, Cardiology, Basel, Switzerland*1. Center for Congenital Heart Disease, Cardiology, University Hospital Inselspital, University of Bern, Switzerland

Introduction: One year after the beginning of the Coronavirus Disease 2019 (COVID-19) pandemic, the evidence on outcomes among adults with congenital heart disease (ACHD) is still limited.

Purpose: We aimed to compare patient characteristics and outcomes between the first and the subsequent COVID-19 waves and to identify overall predictors for complicated disease course among ACHD patients.

Methods: We collected reported COVID-19 cases among ACHD patients followed at 26 tertiary care centers in 10 European countries between March 27,' 2020 and March 25, 2021. Patient characteristics, heart defect complexity and residual problems, medical history, date of diagnosis and course and outcome of COVID-19 were recorded. Cases were stratified into first vs. subsequent COVID-19 waves (cut-off date July 15, 2020). A complicated disease course was defined as hospitalization for COVID-19 requiring ventilation and/or inotropic support, extracorporeal membrane oxygenation or death. Data were reported as median (interquartile range) and counts (percentage).

Results: Overall, 548 cases were included (first wave: n=161; subsequent waves: n=387). Median age 33 (26-44) years, 52% female. Thirty-three patients (6%) had a complicated disease course. Between waves (first vs. subsequent), there were no statistically significant differences related to gender (women 57% vs. 49%, p=0.09), body mass index (BMI) category (p=0.7), heart defect complexity (p=0.08) and residual heart defect-related problems (p=0.6). Patients in the first wave were older, had more often ≥ 2 comorbidities and a complicated disease course (37 vs 33 years, p=0,001; 17% vs. 7%, p=0.0003; and 9% vs. 5%, p=0.04, respectively). The proportion of deaths did not significantly differed between waves (4% vs 2%, p=0.2). A detailed comparison of the above-reported characteristics is depicted in ***table 1***. From multivariable models, adjusted odds ratios (OR) (95% confidence interval) for the prediction of complicated COVID-19 course are depicted in ***table 2***. Main independent predictors for a complicated disease course were: cyanotic heart disease, including unrepaired cyanotic defects or severe pulmonary hypertension with Eisenmenger syndrome (OR 8.49

[3.14-22.94], p <0.001), BMI >25 kg/m2 (OR 3.91 [1.62-9.43], p=0.002), having ≥ 2 comorbidities (OR 2.63 [1.05-6.62], p=0.04) and age per five years (OR 1.21 [1.05-1.42], p=0.01).

Conclusion: Complicated COVID-19 course among ACHD patients is rare. Outcomes in the first wave were worse when compared to subsequent waves, mainly because patients of the first wave were older and had more comorbidities. Age, cyanotic heart disease (including unrepaired cyanotic defects or severe pulmonary hypertension with Eisenmenger syndrome), having ≥ 2 comorbidities and a BMI >25 kg/m^2 were the main predictors for a complicated disease course.

Key words: COVID-19, adult congenital heart disease, outcome.

Table 1. Patient characteristics stratified by coronavirus disease 2019-wave

n = 548 patients	**First wave (n= 161)**	**Subsequent waves (n=387)**	**p**
Female gender (%)	92 (57)	190 (49)	**0.09**
Age (years)	37 (29-47)	33 (25-43)	**0.001**
BMI			**0.7**
<25	100 (62)	253 (66)	
25-30	40 (25)	88 (23)	
>30	21 (13)	44 (11)	
≥ 2 comorbidities (yes)	27 (17)	26 (7)	**0.0003**
Cardiac defect complexity			**0.08**
mild	60 (37)	131 (34)	
Moderate	63 (39)	128 (33)	
severe	38 (24)	128 (33)	
Residual defect-related problems			**0.6**
no problems	60 (37)	172 (44)	
mainly valvular problem	58 (36)	122 (32)	
mainly heart failure	15 (9)	31 (8)	
mainly arrhythmia problems	20 (12)	41 (11)	
pulmonary hypertension	8 (5)	21 (5)	
Complicated disease course	15 (9)	18 (5)	**0.04**
Deaths (only)	7 (4)	9 (2)	**0.2**

Data are median (interquartile range) or number (percentage). BMI= body mass index (in kg/m2)

Table 2. Predictors for complicated coronavirus disease 2019-course

Predictor	Odds ratio	95% Confidence interval	p
Univariate logistic regression			
Sex (male)	0.77	(0.38-1.57)	0.5
Age (per 5 years)	1.39	(1.22-1.57)	<0.001
Cardiac defect complexity (severe)	1.54	(0.75-3.17)	0.2
BMI >25 Kg/m^2	4.41	(2.04-9.52)	<0.001
Cyanotic heart disease or ES	8.02	(3.35-19.20)	<0.001
≥ 2 comorbidities	6.54	(3.0-14.23)	<0.001
Pulmonary arterial hypertension	9.28	(3.82-22.53)	<0.001
COVID-19 wave (first)	2.11	(1.03-4.29)	0.04
Multivariate logistic regression			
Age	1.22	(1.05-1.42)	0.01
Cyanotic heart disease or ES	8.49	(3.14-22.94)	<0.001
BMI >25 Kg/m^2	3.91	(1.62-9.43)	0.02
≥ 2 comorbidities	2.64	(1.05-6.62)	0.04

COVID-19 wave (first)	1.86	(0.84-4.13)	0.1

Total number of events: 33. BMI= body mass index; COVID-19= coronavirus disease 2019; ES= Eisenmenger syndrome