

# Adult congenital heart disease and the coronavirus disease 2019: How to deal with uncertainty

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## Related article

by Lipczyńska et al.

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DOI: 10.33963/KPa2022.0023

### Received:

January 21, 2022

### Accepted:

January 21, 2022

### Early publication date:

January 26, 2022

In the early stages of the COVID-19 pandemic, pre-existing cardiovascular diseases were identified as important predictors for a dismal disease course in case of infection with the novel SARS-CoV-2 [1, 2]. Initially, it was unclear whether mostly young and otherwise healthy adults with congenital heart disease (ACHD) were at similar risk from severe COVID-19 as patients with acquired cardiovascular disease.

To err on the safe side, first experts' opinion-based recommendations on risk stratification for ACHD patients considered an important proportion of patients to be at moderate or high risk. Attention was mainly paid to the anatomical complexity of the congenital heart lesion [3, 4].

In October 2020, Lewis et al. [5] were the first to report outcomes among a single-center cohort of 53 children and adults with congenital heart disease (CHD) suffering from COVID-19. They were also the first to propose that physiological stage rather than cardiac anatomy was predictive of outcomes among ACHD patients in the case of COVID-19. Soon thereafter, this single-center experience was followed by a European multicenter registry addressing risk stratification of ACHD patients in the current pandemic [6]. In this registry, general risk factors (such as age, obesity, and multiple co-morbidities) were associated with an increased risk of complicated COVID-19 course, and patients with cyanotic heart disease, independent of the underlying anatomy, were deemed to be at the highest risk. The importance of the patients' physiological state in predicting

COVID-19 risks in ACHD patients was again confirmed by Broberg et al. [7] in the largest so-far worldwide multicenter study. Again, general risk factors such as diabetes, male sex, increasing body mass index (BMI), and age were found to independently predict poor outcomes among ACHD patients with COVID-19. As reported before, cyanosis, but not cardiac anatomy *per se*, was an independent predictor of death.

In this issue of the *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*), Lipczyńska et al. [8] report COVID-19 cases among 1197 ACHD patients followed at a tertiary care center in Poland. A severe COVID-19 course was defined as either hospitalization requiring oxygen supply, non-invasive or invasive ventilation or circulatory support, or death. This retrospective analysis of patients attending the ACHD outpatient clinic in Warszawa between September 1, 2020 and March 31, 2021 identified 104 patients with COVID-19 confirmed with a positive test (n = 89) or a suspected SARS-CoV-2 infection (n = 15). Overall, five patients had a severe COVID-19 course, two of whom died. Decreased ventricular systolic function and significant valvular stenosis were frequently encountered in ACHD patients with a severe course, but the low number of outcome events preclude a meaningful statistical analysis. None of the general risk factors previously associated with dismal outcomes in the case of COVID-19 in both the general population and ACHD patients (such as older age, male sex, BMI, or comorbidities) predicted the outcome of interest. This result

**Table 1.** Predictors for poor COVID-19-related outcome [5–8]

Risk factor	Lewis et al. COVID-19 cases: n = 53 <sup>a</sup> Outcome events: n = 9	Schwerzmann et al. COVID-19 cases: n = 105 <sup>a</sup> Outcome events: n = 13	Broberg et al. COVID-19 cases: n = 1044 <sup>a</sup> Outcome events: n = 24	Lipczyńska et al. COVID-19 cases: n = 104 <sup>a</sup> Outcome events: n = 5
General				
Age	Univariable OR: 0.98; <i>P</i> = 0.39	Per 5 years Univariable OR: 1.3; <i>P</i> = 0.02	Per year Univariable OR: 1.03; <i>P</i> = 0.03	Univariable OR: 1.00; <i>P</i> = 0.98
Male sex	Univariable OR: 1.51; <i>P</i> = 0.87	Univariable OR: 2.5; <i>P</i> = 0.13	Univariable OR: 5.4; <i>P</i> = 0.002	Univariable OR: 0.26; <i>P</i> = 0.26
Comorbidities	—	≥2 co-morbidities Univariable OR: 7.1; <i>P</i> = 0.002 Multivariable OR: 6.7; <i>P</i> = 0.03	Diabetes Univariable OR: 6.8; <i>P</i> <0.001 eGFR <60 ml/min/1.73 m <sup>2</sup> Univariable OR: 5.1; <i>P</i> = 0.004	Univariable OR: 2.63; <i>P</i> = 0.30
BMI	Obesity Univariable OR: 7.34; <i>P</i> = 0.046	>25 kg/m <sup>2</sup> Univariable OR: 7.2; <i>P</i> = 0.004 Multivariable OR: 16.4; <i>P</i> = 0.001	Univariable OR: 1.08; <i>P</i> = 0.001	Univariable OR 0.93; <i>P</i> = 0.52
ACHD-specific				
CHD-PAH	Univariable OR: 15.25; <i>P</i> = 0.01	—	Univariable OR: 5.9; <i>P</i> <0.001	OR: 4.44; <i>P</i> = 0.11
Cyanotic CHD	—	Univariable OR: 13.2; <i>P</i> = 0.002 Multivariable OR 60.0; <i>P</i> <0.001	Univariable OR: 8.9; <i>P</i> <0.001	—
Physiological stage	Physiologic Stage C Univariable OR: 19.38; <i>P</i> = 0.002	—	Physiological stage C or D Univariable OR: 6.4; <i>P</i> = 0.001 Previous heart failure admission Univariable OR: 7.4; <i>P</i> <0.001	Decreased systemic EF OR: 20.75; <i>P</i> = 0.02 Significant valvar stenosis OR: 20.75; <i>P</i> = 0.02

Abbreviations: ACHD, adult congenital heart disease; BMI, body mass index; CHD, congenital heart defect; EF, ejection fraction; eGFR, estimated glomerular filtration rate; OR, odds ratio

<sup>a</sup>A poor COVID-19-related outcome was defined as follows:

- Lewis et al: death or need for hospitalization, or new or increased respiratory support;
- Schwerzmann et al: hospitalization for COVID-19 requiring non-invasive or invasive ventilation and/or inotropic support, or death;
- Broberg et al: death;
- Lipczyńska et al: either hospitalization requiring oxygen supply, non-invasive or invasive ventilation or circulatory support, or death

was, most likely, another consequence of the small number of outcome events reported in this population.

Remarkably, of 1197 ACHD patients followed during the defined period, 28% had a telemedicine consultation only. In the current pandemic times, this is an important technical help to minimize the number of patients lost to follow-up, and the ACHD healthcare providers of the participating center must be congratulated for this innovative effort.

A comparative overview of previously defined predictors for poor COVID-19-related outcomes including the work by Lipczyńska et al. [8] and other studies is depicted in Table 1. There are important discrepancies between the results. This might be partially attributable to different pandemic waves and virus strains but certainly also to the challenges of collecting a sufficient number of events. When looking closely at the reported severe cases in the present study [8], the two deceased patients had either general risk factors (systemic hypertension and being overweight in the 51 years-old female with repaired tetralogy of Fallot) or both general and ACHD-specific risk factors (cyanotic heart disease and obesity in the 36-year-old female with the unrepaired common arterial trunk). All one can say at this time is that in ACHD patients COVID-19 risks are related to the general health and the physiological state and not the complexity of the defect. The physiological state can

be expressed by functional class or, as in the present study, by quoting ventricular ejection fraction or quantifying valvular disease. Both approaches seem to predict COVID-19 outcomes.

The COVID-19 pandemic has taught the ACHD community two important lessons: single-center efforts, like the present study, are the first and most important step for guiding ACHD patient management. Due to the variety of congenital cardiac defects and repair strategies, ACHD patients are a very heterogeneous population, and in the end, only collaboration among different centers from different countries will facilitate the collection of a sufficiently large number of ACHD cases to make meaningful conclusions. Collaboration is, therefore, the key to success. Secondly, ACHD patients' management that is mainly based on theoretical reasoning might be tempting but is not necessarily the right way to go. In the case of COVID-19 patients, we have realized that the young age of many of our patients is a very protective factor, independent of the underlying defect complexity. Declaring all ACHD patients with complex lesions to be at high risk for COVID-19 complications creates an unnecessary psychological burden to younger patients, some of whom are already struggling with the challenges of living with a congenital cardiac defect. As for other disciplines in cardiology, also ACHD management should be built on evidence whenever possible:

## Article information

**Conflict of interest:** None declared.

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