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Adult congenital heart disease: Special considerations for COVID-19 and vaccine allocation/prioritization

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ABSTRACT

Individuals with the highest risk for adverse outcomes of COVID-19 should be prioritized by the vaccine allocation policies. We have conducted a literature review of published studies, which comprehend congenital heart disease (CHD) and COVID-19, in order to present the overall evidences of both exposure and clinical risk of patients with adult congenital heart disease (ACHD) and to propose a risk profile schema for those patients to be incorporated into vaccine distribution decisions.

Background

The coronavirus disease 2019 (COVID-19) has provoked an overwhelming impact on healthcare systems worldwide, with million of victims to date [1,2]. As things stand, the urgent availability of numerous vaccines is of utmost importance in combating the COVID-19 pandemic.

Individuals with the highest risk for adverse outcomes of COVID-19 should be prioritized by the vaccine allocation policies around the world [2–5].

Diverse factors may influence the risk for adverse outcomes COVID-19-related, not to mention the chances of contagion and the risk for adverse clinical outcomes due to the acute infection.

On that account, we have conducted a literature review of published studies which comprehend congenital heart disease (CHD) and COVID-19, in order to present the overall evidences of both exposure and clinical risk of patients with adult congenital heart disease (ACHD) needed for vaccine allocation efforts, and to propose a risk profile schema for ACHD patients to be incorporated into vaccine distribution decisions.

Adult congenital heart disease

Congenital heart disease (CHD) is the most common global inborn disorder. With an increasing life expectancy, adults with CHD are exposed to acquired diseases, cardiovascular disease and to environmental threats, along with infectious diseases [6].

Different studies have recognized adult-onset cardiovascular disease as a risk factor for mortality in COVID-19 infections [3]. Hence, by the beginning of the COVID-19 pandemic, it was feared this risk might have been further multiplied in patients with CHD, especially when associated with diverse comorbidities such as pulmonary hypertension, heart failure, or in the presence of complex congenital heart disease [6–9].

There are limited data with several knowledge gaps remaining about adult congenital heart disease (ACHD) and potentially adverse outcomes in patients contracting COVID-19 [10].

Moreover, the anatomy, physiology and functional status amongst ACHD patients are varied. For this reason, the risk for poor outcomes from COVID-19 in the very heterogeneous ACHD population remains, albeit poorly specified.

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In this context, Cleary et al. [11] reported a comprehensive review of literature of a total of 94 suspected or confirmed cases from 7 papers [12–18]; of those, the largest published series comes from Italy [12], with 76 patients included. Amongst the 94 reported CHD cases with COVID-19 infection, 79 (84%) were adults whereas 15 (16%) children. Only one death reported from these combined series (mortality just over 1%).

Furthermore, Lewis et al. [19] reported a single-center cohort study from New York City evaluating COVID-19-related outcomes in patients with CHD. From a population of >7000 adults and children under follow-up at their tertiary center, only 53 CHD patients presented with COVID-19-related symptoms over a 4-month period, 43 (81%) of them adults; seven patients (5.7%) died from COVID-19 in this cohort [18].

Broberg et al. [20] reported a study from 58 ACHD centers, including 1044 infected patients: 118 (11%) with single ventricle physiology, 87 (8%) with cyanosis, and 73 (7%) with pulmonary hypertension. Twenty-four COVID-related deaths were reported, and factors associated with mortality consisted of male sex, diabetes, cyanosis, pulmonary hypertension, heart failure.

Finally, Schwerzmann [21] et al. showed that among 105 ACHD patients 13 had a severe disease course and 5 died with general risk factors (age, obesity and multiple comorbidities) resulting associated with an increased risk of mortality.

Accordingly, all the reported studies showed type of ACHD, including single ventricle physiology, was not associated with worse clinical outcomes related to COVID-19. ACHD patients at advanced physiological stage were at highest risk of a moderate/severe course of COVID-19 disease.

However, ACHD patients at advanced physiological stage, in turn were considered, if had one of the following criteria:

- New York Heart Association (NYHA) functional class III or greater;
- hypoxemia (pulse oximetry at rest <90%);
- arrhythmias;
- haemodynamically significant shunt (Qp:Qs ≥ 1.5:1 and/or chamber dilatation in correspondence to shunt);
- moderate/severe aortic dilatation;
- moderate or severe valvular stenosis or regurgitation;
- clinical or laboratory evidence of end-organ failure;
- pulmonary hypertension (mean pulmonary artery pressure ≥25 mmHg);
- Eisenmenger syndrome.

Worldwide literature at present suggests that estimated prevalence of COVID-19 disease amongst ACHD patients and related mortality of ACHD to be low [11–21]. The former may be the result, at least in part, of precautionary shielding. Moreover, the disease does not seem to impact a specific form of CHD.

Furthermore, reduced exposure because of shielding, rather than resistance to infection, and/or incomplete recognition due to the generally mild or asymptomatic COVID-19 disease in ACHD, may in part explain this. ACHD patients are generally a relative young population, which may have an effect on COVID-19 outcome.

Studies published so far [11–21] did not show similar critical respiratory outcomes and/or the higher mortality rates reported in other cardiovascular diseases [2,3]. This would suggest that advanced physiological state and adult-onset cardiovascular risk factors, like older age, obesity, hypertension and diabetes play a pivotal role in COVID-19 mortality, rather than congenital cardiac disease per se [22].

Thus, it is imperative to recognize the clinical characteristics of advanced physiological state of patients with ACHD that may lead to adverse outcomes, including mortality, at this time of ongoing COVID-19 pandemic.

Pulmonary hypertension

Data regarding patients with pulmonary hypertension (PH) are, likewise, limited; it seems, however, that PH carries an increased mortality risk related to COVID-19.

A survey amongst 77 American PH centers showed, even a similar incidence of COVID-19 infection in patients with PH to the general U.S. population (2.9 per 1000 patients), albeit rates of hospitalization and

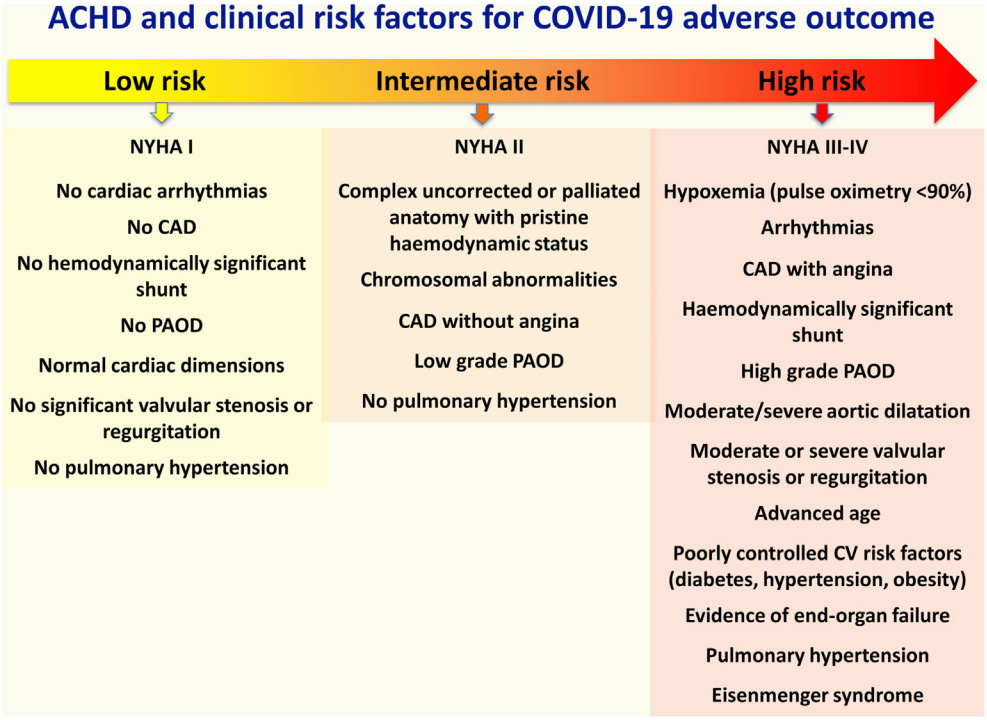

Fig. 1. Risk stratification schema of ACHD patients according to anatomical and physiological patterns. CAD = coronary artery disease; PAOD = peripheral arterial occlusive disease; CV = cardiovascular.

mortality were much higher, at 30% and 12% respectively amongst the former [23].

Although no studies are available at present examining the interaction between PH severity and COVID-19 infection and outcomes, we speculate COVID-19 may augment pulmonary vascular disease through multiple mechanisms including pneumonia - with worsening V/Q mismatch - and hypoxia, hypercapnic vasoconstriction, and/or thrombosis [24]. On the other hand, COVID-19 may also impact, directly, on endothelial cells leading to or accelerating endothelial dysfunction.25 The latter is particularly relevant in patients with haemodinamically significant PH, whereas the pre-existing endothelial dysfunction superimposed by COVID-19 act as a trigger for progressive vasoconstriction and end-organ damage.

Last but not least, it is possible that patients with PH had undergone fewer clinic visits and diagnostic testing because of shielding for COVID-19, potential compromising treatment and care, albeit this is speculative.

Proposed vaccination allocation and prioritization by ACHD clinical risk for COVID-19 adverse outcomes.

Based on literature review, available data and our experience, we propose a vaccine allocation schema (Fig. 1) that describes the major CV clinical risk considerations in the broader and complex context of ACHD.

The schema prioritizes the high risk ACHD subsets, who should receive COVID-19 vaccination without delay.

Physiological status, symptoms including history of heart failure and presence of pulmonary hypertension determine COVID-19 risks and not complexity of underplaying CHD conditions in the ACHD population. All ACHD patients, high or low risk should observe social distance measures and invest on optimizing modifiable risk factors such as obesity, smoking and lack of exercise, which will impact on quality of life and outcomes, the latter whether COVID-19 or not.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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