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COVID-19 vaccination in adults with congenital heart disease: Real-world data from an Italian tertiary centre☆

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ABSTRACT

Background: real-world data on COVID-19 vaccine safety, immunogenicity and acceptance in adults with congenital heart disease (ACHD) are lacking.
Methods: ACHD patients who were offered COVID-19 vaccination from January to June 2021 were included. Data on adverse events, on patients' attitude towards vaccination and antispike IgG titre were retrospectively collected. A group of healthy individuals with similar age and sex undergoing vaccination was included for comparison.
Results: 208 patients followed in a single ACHD tertiary centre (33.3 [26–45] years, 54% male) received COVID-19 vaccine, 65% vaccinated at our institution: 199 (96%) received Pfizer–BioNTech BNT162b2 vaccine, 4 (2%) Moderna-1273 and 5 (2%) AstraZeneca–ChAdOx1. Median follow-up after vaccination was 79 [57–96] days. No major adverse event was reported and the incidence of minor events was not different between ACHD patients and the control group. One patient was diagnosed with acute pericarditis. There were two deaths unrelated to the vaccine during follow-up. Three (1.5%) vaccinated patients tested positive for COVID-19. Antispike IgG titre, available in 159 (76%) patients, was 1334 [600–3401] BAU/ml, not significantly different from the control group ($p=0.2$). One patient with Fontan failure was seronegative. Advanced physiological stage was associated with lower antibody response, independently from previous viral exposure ($p<0.0001$). Fourteen percent refused COVID-19 vaccination at our institution. However, 50% of vaccinated patients declared to have been influenced by the discussion with the ACHD cardiologist and 66% of those vaccinated in situ reported that undergoing COVID-19 vaccination at the ACHD centre made them feel safer.
Conclusion: COVID-19 vaccines appear safe in ACHD with satisfactory immunogenicity. However, the most vulnerable patients showed lower antibody response. ACHD team may play a key role in vaccine acceptance.

1. Introduction

Coronavirus disease-2019 (COVID-19) has had a devastating impact worldwide, claiming nearly 4 million victims as of June 2021 [1]. Universal COVID-19 vaccination will be the keystone in the fight against the pandemic. Patients with cardiovascular disease [2], including adults with congenital heart defects (ACHD), are often considered to bear a higher risk of adverse outcome in case of infection, and it has been suggested that they should be prioritized by vaccine allocation policies [3]. Although the approval trials of most recently licensed vaccines have shown good safety profile with high efficacy [4,5], real-world data are still lacking. Thus, patients with underlying heart disease may opt out of vaccination, fearing adverse cardiac effects from doing so.

The Italian Government launched a nationwide vaccination campaign

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started on December 31, 2020: vaccines were offered to the entire population according to a priority order, accounting for vaccines availability and individual vulnerability to COVID-19. In particular, healthcare and education workers, residents of long-term care facilities and vulnerable subjects, defined as patients>80 years, in NYHA class III-IV and those with genetic syndromes were initially targeted [6] and invited to undergo COVID-19 vaccine at local health districts.

With the present study, we aimed to describe the current state of COVID-19 vaccination among ACHD patients followed at our tertiary centre, investigating vaccine safety, immunogenicity and patients' attitude towards vaccination in this complex population.

2. Methods

2.1. COVID-19 vaccination at the ACHD tertiary centre

From March 17, 2021, vulnerable ACHD patients followed at our tertiary ACHD centre and not yet vaccinated locally were offered mRNA-based COVID-19 vaccines in a dedicated unit with specialized personnel and availability of anaesthesiologists and cardiologists experienced in ACHD care. In addition to the subjects meeting the national "vulnerability"criteria, patients with the following characteristics were prioritized at our centre: univentricular physiology, systemic right ventricle, ejection fraction<40%, severe valvular defects and ventricular dilation/dysfunction or awaiting cardiac surgery. In agreement to local guidelines, the second dose was not administrated to those with previous severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) infection and adequate response at 3 weeks and those with SARS-CoV-2 infection in the last 3 months [8]. Patients with previous history of any allergies were pre-treated with antihistaminic and corticosteroids. Patients undergoing COVID-19 vaccination were invited to contact the ACHD team in case of symptoms following COVID-19 vaccination and were instructed to fill in the adverse event report form, according to the European legislation [7]. Blood samples were routinely obtained 3 weeks following the last dose in order to quantify the antibody response in this population and determine previous viral exposure.

2.2. Patients selection, data collection

Consecutive ACHD patients aged≥16 years who were offered COVID-19 vaccine either at our institution or locally between January and June 2021 were included. Demographic data, data on previous medical history, vaccine type, side effects, antibody titre and general attitude towards COVID-19 vaccines were retrospectively collected from patients' electronic records. A group of healthy volunteers with similar age and sex who underwent COVID-19 vaccination was enrolled among the health personal working at our Institution as a control. Informed consent was obtained from each patient before study inclusion. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institutional ethics committee.

2.3. Laboratory procedures

All analytical procedures were performed at the Department for Laboratory Medicine, Monaldi Hospital. Sera were stored at 2–10 °C for <2 days within the Monaldi Hospital facility for the storage of biomaterial with certified quality management (ISO9001:2015). CE-marked Roche Elecsys®Anti-SARS-CoV-2 Sbinding assay was used. This is an electrochemiluminescence sandwich immunoassay which allows to obtain both qualitative detection of SARS-CoV-2 antibodies against the nucleocapsid antigen (indicating previous exposure to SARS-COV2) and quantitative detection of antibodies directed against the viral spike protein. The manufacturer states intra- and interassay precision of 1–3% and positive agreement with a virus pseudo-neutralization assay of 92% (95%CI64–100%) with a specificity of 99.98% (95%CI 99.91–100%). The quantification range is between 1 and 12500 BAU/mL. Results ≥ 1BAU/mL were considered positive, while a titre<100BAU/mL was considered as poor antibody response.

2.4. Statistical analysis

Statistical analysis was carried out using R version 4.0.5. Continuous variables were reported as mean ± SD or median [IQR], according to data distribution. Comparisons between groups were assessed with the Student *t*-test or with Wilcoxon rank-sum test. Categorical variables were presented as frequencies (percentage of total). Differences in proportions were evaluated with χ^2. Univariate and multivariable linear regression model was derived with the Spearman method using the log of IgG values as the dependent variable. Variables significant on univariate analysis were included in the multivariable model. P-value<0.05 was considered statistically significant.

3. Results

3.1. Study population and vaccination modalities

As of June 2021, 208 ACHD patients received COVID-19 vaccine: 73 (35%) locally and 135 (65%) at our institution. One-hundred and ninety-eight (95%) received 2 doses according to vaccination schedule and 10 out of 15 patients with previous SARS-COV2 infection received only the first dose. The type of vaccine was Pfizer–BioNTech BNT162b2 mRNA vaccine in 199 (96%) patients, Moderna mRNA-1273 vaccine in 4 (2%) and AstraZeneca–Oxford ChAdOx1nCov-19 vaccine in 5 (2%). Clinical and demographics data are summarized in Table 1: there was a prevalence of patients with complex disease (52%) and advanced physiological stage (79% in stage C-D as defined by AHA/ACC ACHD guidelines [8]). Forty-two patients (20%) had univentricular physiology and 67 (32%) had a systemic right ventricle. A minority of patients with simple defects (1%), physiological stage A (1%) or good exercise tolerance (3% in NYHA class I) were prioritized in the vaccine campaign as they met additional risk criteria (genetic disease, health-care and education workers, residents of long-care facilities). Thirty-three (16%) patients declared previous allergies and antiallergic prophylaxis was performed in 27 patients.

Two fully vaccinated patients and one with the first vaccine dose were tested positive for COVID-19: they reported only mild symptoms and, in the latter case, the second dose was not administrated.

3.2. Adverse events

The median follow-up after vaccination completion was 79 [57–96] days. Participants reported symptoms after the first and second dose in 78 and 37% of cases, respectively. However, symptoms duration was always limited. Post-vaccination symptoms are summarized in Table 2. No allergic reactions occurred. The most common events included pain at the site of injection, headache, fever, muscle pain, gastrointestinal disturbs, fatigue and dizziness. After the first dose, two patients developed an urticarial rash on the back, neck and abdomen which resolved after treatment with corticosteroids and antihistamines. Neither of them reported previous allergic history, however, both were advised on antiallergic prophylaxis before the second dose. Two patients demonstrated transient inflammatory markers increase. In one of them, raised C-reactive protein (CRP) associated with the finding of severe pulmonary regurgitation on a recently implanted Melody valve, triggered further investigations which ruled out the diagnosis of infective endocarditis. One patient complaining of chest pain was diagnosed with acute pericarditis 4 days following the second dose with BNT162b2 mRNA vaccine and was successfully treated with non-steroidal anti-inflammatory drugs.

During the study period, 6 (2%) patients were admitted to our institution for urgent care during post vaccination follow-up: 4 in the week following the first dose of vaccine and 1 after 85 days from the second dose. The reasons for non-elective hospitalization were: complete diagnostic work-up to rule out pulmonary valve infection, atrial fibrillation with rapid ventricular response, recurrent atrial thrombosis with

Table 1
Demographics and clinical characteristics of ACHD vaccinated patients.

Age (years)	33.3 [26–45]
Sex (male)	112 (54%)
Disease complexity/main cardiac diagnosis	- *3(1%) Simple:* ASD - *97(47%) Moderate:* 3 aortic coarctation 17 AVSD 3 VSD 2 PAPVD 35 TOF 11 Ebstein 5 PS 6 MVD 9 BAV/AS 3 sub/supravalvular AS 3 Shone syndrome - *108(52%) Complex:* 6 PA 38 TGA 25 ccTGA 8 DORV 9 DILV 1 DIRV 10 TA 3 HLHS 2 univentricular heart indeterminate type 5 heterotaxy syndrome 1 unrepaired AVSD
Physiological stage	A→ 3 (1%) B →41 (20%) C →155 (75%) D→ 10 (5%)
NYHA class	1 → 7 (3%) 2 → 91 (44%) 3 → 108 (52%) 4 → 2 (1%)
Genetic disorders	29 (14%): 19 Down syndrome 1 Noonan syndrome 1 Partial 6q trisomy 1 Turner syndrome 1 Myhre syndrome 2 Williams syndrome 1 Kartagener syndrome 1 De George syndrome 2 unknown genetic disorder
Comorbidities	58 (28%) 7 obesity 5 diabetes 10 dyslipidemia 7 hypertension 2 coronary artery disease 1 peripheral arterial atherosclerosis 1 thrombotic diathesis 7 dysventilation syndrome 4 hepatitis 16 thyroid dysfunction 1 renal failure 7 neurologic/psychiatric disease 3 extracardiac malformations 1 Sjogren syndrome 1 pituitary adenoma 1 dysferlinopathy
Previous thromboembolism	4 embolic stroke 2 intracardiac thrombosis 1 pulmonary embolism 1 deep venous thrombosis
Number of previous cardiac surgeries	1 → 84 (40%) 2 → 43 (21%) 3 → 40 (19%) 4 → 4 (2%)
Cyanosis at rest	17 (8%)
Fontan palliation	38 (18%)
Univentricular physiology	42 (20%)
sRV	67 (32%)
EF (%)	50 ± 11
At least moderate valvular disease	146 (70%)
Previous hospitalization for HF	51 (25%)
Nt-proBNP (pg/ml)	181 [90.5–365]
PAH	3 (1.4%)
Chronic oxygen supplementation	3 (1.4%)
Medications at last visit	Betablockers: 112 (54%) ACEi/ARB: 132 (64%) Antiarrhythmic: 49 (24%) Diuretics: 81 (40%) Antiplatelets: 44 (21%) Anticoagulation: 67 (32%)
PMK	28 (13%)
ICD	12 (6%)

Abbreviations: ACEi = angiotensin converting enzyme inhibitor, ARB = aldosterone receptor blockers, ASD = atrial septal defect, AS = aortic stenosis, AVSD = atrioventricular septal defect, BAV = bicuspid aortic valve, ccTGA = congenitally corrected transposition of the great arteries, DILV = double inlet left ventricle, DIRV = double inlet right ventricle, DOLV = double outlet left ventricle, DORV = double outlet right ventricle, EF = ejection fraction, HF = heart failure, HLHS = hypoplastic left heart syndrome, ICD = implantable defibrillator/cardioverter, MVD = mitral valve disease, TA = tricuspid atresia, TGA = transposition of the great arteries, TOF = tetralogy of Fallot, PA = pulmonary atresia, PAH = pulmonary arterial hypertension, PAPVD = partial anomalous pulmonary venous drainage, PMK = pacemaker, PS = pulmonary stenosis, sRV = systemic right ventricle, VSD = ventricular septal defects.

Table 2
COVID-19 vaccines adverse events in ACHD patients.

	First vaccine dose N = 208	Second vaccine dose N = 198
Adverse events	155 (75%)	103 (50%)
Symptoms duration range	1–15 days	1–14 days
Local reactions		
Pain	136 (65%)	60 (29%)
Swelling	20 (10%)	6 (3%)
Systemic reactions		
Fever	11 (5%)	21 (10%)
Headache	20 (10%)	29 (14%)
Myalgia/Arthralgia	15 (7%)	26 (13%)
Gastrointestinal symptoms	14 (7%)	18 (9%)
Fatigue/malaise	6 (3%)	13 (6%)
Diffuse skin rush	2 (1%)	0
Others	2 CRP raise 4 dizziness 1 paresthesia 1 pharyngodynia 1 herpes labialis 3 palpitations 1 anosmia 1 chills	1 late period 2 hypotension 1 hypertensive peak 1 dyspnea 1 pharyngodynia 1 chest pain 1 flu-like 1 chills
Medications	15 (7%) paracetamol 2 antihistamines+corticosteroids 1 non-steroidal anti-inflammatory drugs	24 (12%) paracetamol 2 non-steroidal anti-inflammatory drugs

paradoxical embolism in a patient with Fontan palliation, decompensated heart failure in a patient with systemic right ventricle and another with Fontan failure. At further investigation, atrial thrombosis and high ventricular rate in atrial fibrillation appeared both attributable to of oadherence to treatment. Two fully vaccinated patients died in-hospital 88 and 82 days after the second dose for causes unrelated to the vaccine: one patient with preexisting Fontan failure died from advanced heart failure and one patient from procedural complications following a percutaneous pulmonary valve implantation.

3.3. Antibody response

Antispike IgG titre after a median of 25 [21–34] days from the last dose was available for 159 (76%) patients. The median antispike IgG titre was 1334 [600–3401] BAU/ml. One (0.6%) patient with Fontan palliation and protein-losing enteropathy was seronegative and in 7 (3%) the antispike titre was <100 BAU/ml. Clinical details of patients with poor antibody response are summarized in Table 3. Twenty-two out of 159 (14%) showed also positive antinucleocapsid antibodies, demonstrating previous SARS-COV2 exposure. Seventeen of them (77%) did not report a history of known previous COVID-19 infection, suggesting mildly symptomatic disease.

Using linear regression model with the log IgG values as dependent variable, antispike titre was related to previous viral exposure, defined as either history of SARS-COV2 infection or seropositivity for antinucleocapsid antibodies, and advanced physiological stage on both univariate and multivariable analysis (Table 4).

3.4. Vaccine perception and hesitancy in ACHD patients

Overall, 157 ACHD patients were offered COVID-19 vaccination at our institution. Twenty-two of them (14%) refused the vaccine even after discussion with the ACHD team (clinical details are summarized in Table 5). Patients rejecting the vaccination had similar age (p = 0.8), sex (p = 0.5), and disease complexity (p = 0.08) compared with the study population. Data on vaccine attitude were available for 163 (78%) out of 208 vaccinated patients: 28% appeared to have concerns regarding vaccine safety before discussing it with their general practitioner or cardiologist, 30% reported being scared of potential effects of the vaccine on their cardiac disease and 50% were at least partially influenced by the discussion with their ACHD cardiologist in their decision to undergo COVID-19 vaccination. Sixty-six percent of those vaccinated in situ declared that undergoing vaccine at the ACHD centre made them feel safer.

3.5. Comparison with healthy volunteers

Ninety-four healthy volunteers (16% with previous diagnosis of COVID-19 infection) vaccinated with Pfizer–BioNTech BNT162b2 mRNA vaccine were enrolled. The control group was not significantly different from the study population for age and sex (31 [34–58] years, 54% male, p = 0.6 and 0.8 respectively). Controls showed similar prevalence of symptoms after the first dose of vaccine compared with ACHD patients (50 = 68% vs 75%,p = 0.2). However, a higher proportion of controls complained of symptoms following the second dose (58 = 78% vs 50%,p = 0.0001). Anti-spike titre measured at 27 [23–30] days from vaccination was not significantly different compared to the study population (1196 [827–2040] BAU/ml; p = 0.2; Fig. 1).

Table 4
Univariate and multivariable analysis for Log IgG Values.

Univariate linear regression model		
	β (95% CI)	p-value
Age	−0.007 (−0.02 to 0.01)	0.4
Sex (male)	0.15 (−0.35 to 0.67)	0.5
Time from vaccination (days)	−0.009 (−0.02 to 0.004)	0.2
Disease complexity	0.36 (−0.1 to 0.82)	0.12
Fontan	−0.26 (-0.8 to 0.34)	0.39
Physiological stage C-D	−0.22 (-0.79 to 0.34)	0.43
Physiological stage D	−2.19 (−3 to −1.29)	<0.0001
Genetic disorder	496 (−1094 to 2087)	0.5
Hospitalization for heart failure	−0.24 (−0.77 to 0.29)	0.37
Systemic right ventricle	0.25 (−0.23 to 0.73)	0.3
Previous viral exposure	1.9 (1.3–2.4)	<0.0001
Nt-proBNP	7.2 (−0.001 to 0.01)	0.58
Multiple linear regression model		
Previous viral exposure	1.8 (0.27)	<0.0001
Physiological stage D	−1.9 (0.4)	<0.0001
Multiple R-squared 0.34 p-value <0.0001		

Table 5
Demographics and cardiac diagnosis of ACHD who rejected vaccine.

N = 22	
Age	38.8 ± 17
Sex (male)	12 (54%)
Disease complexity/main cardiac diagnosis	- *8(38%) Moderate:* 4 AVSD 1 PAPVD 1 TOF 1 PS 1 MVD - *15(72%) Complex:* 4 PA 3 TGA 6 ccTGA 2 TA 1 univentricular heart indeterminate type
Previous SARS-COV2 infection	2 (1%)

Abbreviations: AVSD = atrioventricular septal defect, ccTGA = congenitally corrected transposition of the great arteries, MVD = mitral valve disease, TA = tricuspid atresia, TGA = transposition of the great arteries, TOF = tetralogy of Fallot, PA = pulmonary atresia, PAPVD = partial anomalous pulmonary venous drainage, PS = pulmonary stenosis.

4. Discussion

Certain ACHD patients bear an increased risk of death from COVID-19. An international multicentre study including 1044 infected ACHD patients showed that cyanosis, pulmonary hypertension, renal failure,

Table 3
Clinical characteristics of ACHD patients with poor antibody response.

	Age	Sex	Diagnosis	Disease Complexity/ Physiological stage	HF	Vaccine type	IgG titre (BAU/ml
1	32	F	TA post Fontan PLE	3/D	1	Pfizer–BioNTech BNT162b2	0.4
2	27	F	TGA post Mustard repair	3/C	1	Pfizer–BioNTech BNT162b2	95
3	49	M	TOF repair	2/D	1	Pfizer–BioNTech BNT162b2	8
4	40	F	TOF repair	2/C	0	Pfizer–BioNTech BNT162b2	77.7
5	20	M	DILV post Fontan PLE	3/D	1	Pfizer–BioNTech BNT162b2	26.6
6	23	F	AVSD repair Down Syndrome	2/C	0	Pfizer–BioNTech BNT162b2	96.8
7	32	M	Pulmonary and mitral stenosis	2/C	1	Moderna mRNA-1273	62.2
8	58	M	TOF repair	2/C	0	Pfizer–BioNTech BNT162b2	94.2

Abbreviations: AVSD = atrioventricular septal defect, DILV = double inlet left ventricle, HF = history of decompensated heart failure, PLE = Protein-losing enteropathy, TA = tricuspid atresia, TGA = transposition of the great arteries, TOF = tetralogy of Fallot.

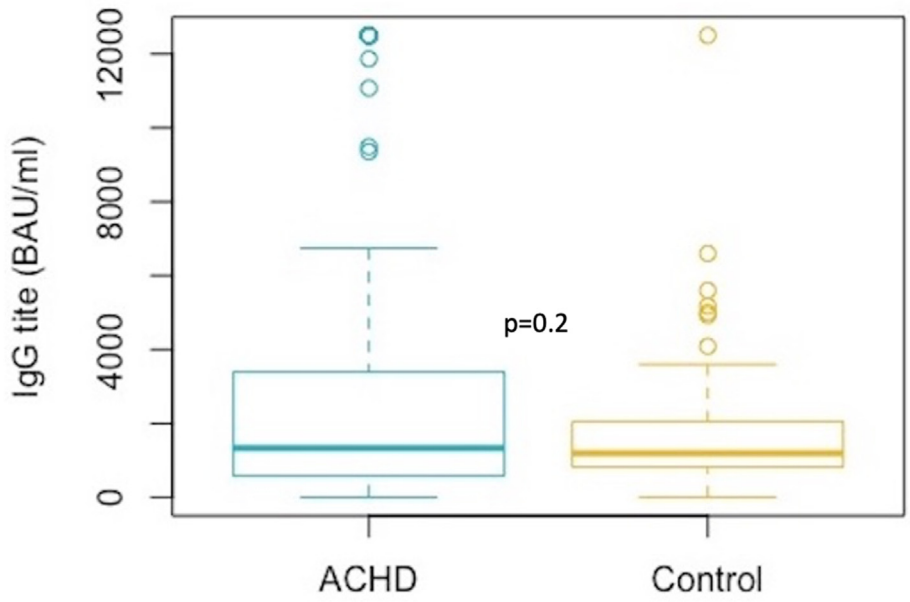

Fig. 1. Boxplot showing the antispike IgG titre in ACHD patients (green) and controls (yellow).

physiological stage and previous hospital admission for heart failure were associated with the risk of death [9]. Accordingly, several scientific statements recommended to prioritize ACHD patients in the vaccine allocation strategy [3,10,11]. However, the current approach to COVID-19 vaccination inACHD patients is mainly based on the vaccines trial data. Herein, we report the first results of an observational study conducted at an ACHD tertiary centre during the COVID-19 pandemic demonstrating the safety and immunogenicity of COVID-19 vaccines in this complex population.

4.1. COVID-19 vaccines safety in ACHD

Our results provided reassuring data for a good safety profile of the vaccines, with most adverse events being transient and mild, similarly to what has been previously reported in the general population [12]. In particular, in our cohort the proportion of subjects reporting adverse events after the second dose was significantly lower in the ACHD group. This might suggest a tendency of ACHD patients to under report mild symptoms in view of their experience of multiple hospital admissions and repeated invasive procedures.

Post-vaccination acute pericarditis and myopericarditis, previously described following mRNA-based COVID-19 vaccination [13,14] might be a particularly fearsome event in ACHD population, especially when presenting with impaired systolic function. In our cohort, the single case of acute pericarditis reported only mild symptoms and made a full remission. Therefore, suspicion should be raised in case of suggestive symptoms during postvaccination surveillance, and patients should be invited to seek early medical attention when new symptoms occur.

Interestingly, we found a transient increase of the inflammatory markers postvaccination in 2 cases. As vaccines are devised to promote an immune response, a transient CRP raise may be expected after vaccination. This potentially confounding factor should be kept into consideration during follow-up of ACHD patients, who are at high risk of systemic infections.

Another emerging concern is the risk of thrombotic events [15,16], especially in ACHD patients who are already prone to their occurrence. Despite the absence of such events in our cohort, no definite conclusions should be drawn based on our data, as only a minority of patients received adenovirus-based vaccines which have been associated with thrombotic risk [19,20].

Other rare adverse events were limited in number, required medical treatment in a small proportion of cases and did not seem to have relevant consequences.

4.2. Immunogenicity

Most ACHD patients in our study showed a satisfactory response with a median antispike titre comparable to the control group. Only 1 seronegative case was demonstrated at 3 weeks from the second dose in a patient with Fontan failure. Other complex ACHD patients showed a flat antibody response in 3% of tested cases. Similarly to what has been reported in the general population [17,18], ACHD patients with COVID-19 pre-existing immunity developed a higher antibody response. Moreover, our results suggested that most vulnerable ACHD patients may develop lower anti-spike IgG titre, regardless of previous viral exposure. As in our cohort patients in physiological stage C were mainly those with univentricular heart and advanced heart failure, our findings are consistent with the profound immune abnormalities, which are typically described in this population, including low immunoglobulin levels and lymphopenia [19,20]. Furthermore, it is interesting to note that despite multiple risk factors for severe disease in case of viral exposure, 14% of patients with no history of known SARS-COV2 infection had positive nucleocapsid antibodies, suggesting mildly symptomatic disease.

4.3. Vaccine acceptance

Although the speed and impact of the pandemic justifies a proactive approach in at-risk population, ACHD patients and their caregivers need to make a decision on accepting vaccination based on limited evidence and a hesitant attitude towards COVID-19 vaccination may be expected in some cases [21,22]. Since the beginning of the national vaccination campaign, ACHD patients followed at our centre were strongly encouraged to undergo COVID-19 vaccination during both in person and remote consultations [23]. In our study population, only a small minority of patients rejected the vaccine. This is likely the effect of the health-related education received since childhood. Moreover, data collected during the clinic highlightened the crucial role of the ACHD team in the patients' vaccination journey. Vulnerable patients might be more willing to undergo COVID-19 vaccination in a “safe” setting with specialized personnel and ACHD expertise. Therefore, patients’ education including discussion on the importance of the vaccination during the clinical

consultation as well as COVID-19 vaccines administration in situ at the ACHD tertiary centre, where patients are and feel cared for, may improve vaccine acceptance.

4.4. Limits

Our study is limited by the single-centre design, limited sample size and highly heterogeneous study population. However, our data reflect the case mix of the most vulnerable patients attending our ACHD centre. Other limitations include the lack of cellular immunity and neutralization assay testing. However, anti-spike titers were shown to be strongly correlated to neutralization levels [24]. Moreover, most ACHD patients underwent COVID-19 vaccination with the Pfizer–BioNTech BNT162b2 mRNA vaccine. Therefore, the safety data herewith reported are mainly related to this type of vaccine. Further research into the clinical relevance of antibody titers and their durability is required.

5. Conclusions

Our study provides the first real-world evidence of COVID-19 vaccines safety and immunogenicity in ACHD patients. Vaccine administration was low risk, and avoidance of vaccination based on fears of vulnerability due to underlying heart disease seems unjustified from this experience. ACHD patients with advanced physiological stage may develop lower antibody response regardless of previous viral exposure. Furthermore, the ACHD team may play a key role in vaccine acceptance in this vulnerable population.

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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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