Cardiology in the Young

cambridge.org/cty

Mid-term follow-up after COVID-19 vaccination in adults with CHD: a prospective study

Flavia Fusco[1], Giancarlo Scognamiglio[1], Anna Selvaggia Roma[1], Massimiliana Abbate[1], Giovanni Papaccioli[1], Assunta Merola[1], Michela Palma[1], Nunzia Borrelli[1], Rosaria Barracano[1], Anna Correra[1], Nicola Grimaldi[1], Giovanni Domenico Ciriello[1], Maurizio D'Abbraccio[2], Cristina Scavone[3], Annalisa Capuano[3] and Berardo Sarubbi[1]

[1]Adult Congenital Heart Disease Unit, AO dei Colli – Monaldi Hospital, Naples, Italy; [2]Vaccination Unit for Vulnerable Patients, AO dei Colli – Cotugno Hospital, Naples, Italy and [3]Section of Pharmacology "L. Donatelli", Department of Experimental Medicine, University of Campania "LuigiVanvitelli", Naples, Italy

Original Article

Cite this article: Fusco F, Scognamiglio G, Roma AS, Abbate M, Papaccioli G, Merola A, Palma M, Borrelli N, Barracano R, Correra A, Grimaldi N, Ciriello GD, D'Abbraccio M, Scavone C, Capuano A, and Sarubbi B (2023) Mid-term follow-up after COVID-19 vaccination in adults with CHD: a prospective study. *Cardiology in the Young* **33**: 2574–2580. doi: 10.1017/S1047951123000689

Received: 10 January 2023
Revised: 20 February 2023
Accepted: 13 March 2023
First published online: 11 April 2023

Keywords:
COVID-19; Adult CHD; vaccination; coronavirus disease 2019; prospective study

Author for correspondence:
Dr F. Fusco, MD, Adult Congenital Heart Disease Unit, Monaldi Hospital, Via Leonardo Bianchi, 80131 Naples, Italy. Tel: +390817064206; Fax: +390817062501.
E-mail: flavia.fusco@ospedalideicolli.it

Abstract

Background: Long-term data on COVID-19 vaccine safety, immunogenicity, and acceptance in adults with CHD are lacking. *Methods:* This is a prospective study including adults with CHD patients undergoing COVID-19 vaccination from January 2021 to June 2022. Data on adverse events, antispike IgG titre, previous or subsequent COVID-19 infection, booster doses, and patients' attitude towards vaccination were collected. *Results:* Four hundred and ninety CHD patients (36 ± 13 years, 53% male, 94% with moderate/complex defects) were prospectively included: 433 (88%) received a Pfizer–BioNTech mRNA vaccine, 31 (6%) Moderna mRNA vaccine, 23 (5%) AstraZeneca–Oxford ChAdOx1 nCov-19 vaccine, and 3 (0.6%) Janssen Vaccine; 310 (63%) received a booster dose. Median follow-up after vaccination was 1.53 [1.41–1.58] years. No major adverse event was reported. Eighty-two fully vaccinated patients contracted COVID-19 during follow-up after a median of 5.4 [4.3–6.5] months from the last dose. One patient with Ebstein's disease died from severe COVID-19. Symptoms' duration in patients who tested positive after vaccination was significantly shorter than in the group tested positive before vaccination (5.5 [3–8] versus 9 [2.2–15] days, $p = 0.04$). Median antispike IgG titre measured in 280 individuals (57%) at a median of 1.4 [0.7–3.3] months from the last dose was 2381 [901–8307] BAU/ml. Sixty patients (12%) also showed positive antinucleocapsid antibodies, demonstrating previous SARS-COV2 exposure. Twenty-nine percent appeared to have concerns regarding vaccine safety and 42% reported fearing potential effects of the vaccine on their cardiac disease before discussing with their CHD cardiologist. *Conclusion:* COVID-19 vaccines appear safe in the mid-term follow-up in adults with CHD with satisfactory immunogenicity and reduction of symptoms' duration in case of infection.

Coronavirus disease 2019 (COVID-19) pandemic has dramatically influenced our lives and healthcare provision worldwide. The rapid deployment and administration of highly effective COVID-19 vaccines have boosted the expectation of definite control of the pandemic.[1,2] Nevertheless, although 68% people worldwide have already received at least one dose of COVID-19 vaccine to date,[3] evidence of only moderate protection against infection with new viral variants[4,5] has tempered that expectation, giving rise to a new wave of uncertainties and fear. Adults with CHD represent a population vulnerable to intercurrent infections, especially those with complex defects and significant cardiac sequelae who have been shown at higher risk of adverse outcomes in case of COVID-19 infection.[6] In Italy, a nationwide vaccination campaign 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. We have previously described the early effects of COVID-19 vaccination campaign in a limited number of adult CHD patients.[7] In this rapidly changing global scenario, we aim to describe the current state of COVID-19 vaccination including booster dosage administration, hypothesising vaccine safety at a longer follow-up and protection against COVID-19 infection among the CHD population, also highlighting fear and vaccine hesitancy among these patients with specific focus on effects on their CHD.

Methods

Patients selection and data collection

This is a prospective observational study carried out from January 2021 to June 2022 and including all consecutive CHD patients aged ≥16 years attending the outpatient clinic of the tertiary centre for Adult Congenital Heart Disease at Monaldi Hospital (Naples, South Italy). As previously described,[7] at our centre CHD patients with univentricular physiology, systemic right ventricle, ejection fraction <40%, severe valvular defects, and ventricular dilation/dysfunction or awaiting cardiac surgery were considered "most frail" and were therefore offered COVID-19 vaccine in our dedicated Unit in an ambulatory setting with specialised personnel and availability of anaesthesiologists and cardiologists experienced in CHD care. Data on COVID-19 infection (either before or following vaccination), COVID-19 vaccines including booster doses and any suspected or confirmed adverse events were prospectively collected during each clinical evaluations. Adverse events following immunisation are defined as "any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine".[8] Demographic data, data on previous medical history including previous infection, and data on vaccine type and adverse events (type of event, symptoms' duration, and concomitant medication) were prospectively collected from patients' electronic records. Missing data in patients' electronic records were collected by phone calls by the CHD team. Patients undergoing COVID-19 vaccination either locally or at our Institution were invited to contact the CHD team in case of any symptom's occurrence during the following weeks and were instructed to fill in the adverse event report form, according to the European legislation.[9] Blood samples were routinely obtained during the first clinical evaluation within 4 months from the last dose administration whenever possible, in order to quantify the antibody response expressed as antispike IgG titre and determine an eventual previous viral exposure. CE-marked Roche Elecsys® Anti-SARS-CoV-2 S binding assays were used. This is an electrochemiluminescence sandwich immunoassay that allows to obtain both qualitative detection of SARS-CoV-2 antibodies against the nucleocapsid antigen, which indicates previous exposure to SARS-CoV2 and quantitative detection of antibodies directed against the viral spike protein. The manufacturer states intra- and inter-assay precision of 1–3% and positive agreement with a virus pseudo-neutralisation assay of 92% (95% CI 64–100%) with a specificity of 99.98% (95% CI 99.91–100%). The quantification range is between 1 and 12,500 BAU/mL. Moreover, patients' attitude towards COVID-19 vaccination was explored with a questionnaire (Table 1 Supplementary material). Post-vaccination data including COVID-19 infection and symptoms duration were routinely collected during routine outpatient clinic and retrieved from patients' electronic medical records. The authors assert that all procedures contributing to this work comply with Helsinki Declaration of 1975, as revised in 2008, and written informed consent was obtained from participants before study inclusion. Study protocol was approved by the Ethic Committee of the Spallanzani Hospital, in agreement with special legislation from the Italian Medicine Agency for prospective studies regarding COVID-19.[10]

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. P-value < 0.05 was considered statistically significant.

Results

Study population

As of June 2022, 490 CHD (36 ± 13 years, 53% male) patients were enrolled. Clinical and demographics data are summarised in Table 1: there was a prevalence of patients with moderate and complex disease (94%) and advanced physiological stage (63% in stage C–D as defined by the 2018 American Heart Association guidelines for the management of adults with CHD[11]). Forty-four (9%) had univentricular physiology and 99 (20%) had a systemic right ventricle. Forty-seven (9.5%) patients had a history of symptomatic COVID-19 infection 4.3 [1–5.2] months before the first dose of vaccination, mainly presenting with mild symptoms with a median duration of 9 [2.2–15] days. Of them, only one required hospitalisation

COVID-19 vaccination

The primary vaccination cycle consisted of two doses in 457 (93%) patients and one dose in 33 (6%) due to recent SARS-CoV2 infection or administration of the Janssen Vaccine. Of them, 301 (61%) received a booster dose following at least 120 days from primary vaccination completion. The type of vaccine administered in the primary vaccination series was Pfizer–BioNTech mRNA vaccine in 433 (88%) patients, Moderna mRNA vaccine in 31 (6%), AstraZeneca–Oxford ChAdOx1 nCov-19 vaccine in 23 (5%), and Janssen Vaccine in 3 (0.6%). COVID-19 vaccination was administered in our Unit to 110 (22%) patients. Ten (2%) received a mixed vaccine regimen. M-RNA vaccines were administered as booster dose after at least 6 months from the last dose. Specifically, 230/310 (74%) received Pfizer–BioNTech vaccine and 80/310 (26%) received Moderna vaccine.

Follow-up after COVID-19 vaccination and antibody response

The median follow-up after the first dose was 1.53 [1.41–1.58] years. Adverse events were reported by 59, 51, and 40% of participants after the first, second, and booster dose, respectively (Table 2). However, symptoms were mainly mild. The most common adverse events included pain at the site of injection, headache, fever, muscle pain, gastrointestinal disturbs, fatigue, and dizziness. No major allergic reactions occurred. One patient complaining of chest pain was diagnosed with acute pericarditis 4 days after the second dose with Pfizer–BioNTech vaccine and was successfully treated with non-steroidal anti-inflammatory drugs. During the study period, four patients with complex disease (three univentricular heart with Fontan palliation and one with transposition of the great arteries following atrial switch repair) died from cardiac reasons, unrelated to COVID-19 vaccination. Antispike IgG titre obtained after a median of 1.4 [0.7–3.3] months from the last dose was available for 280 (57%) CHD patients. The median antispike IgG titre was 2381 [901–8307] BAU/ml. Sixty (12%) patients also showed positive antinucleocapsid antibodies, demonstrating previous SARS-COV2 exposure. However, 35 out of 60 patients with positive antinucleocapsid antibodies did not

https://doi.org/10.1017/S1047951123000689 Published online by Cambridge University Press

Table 1. Demographics and clinical characteristics of the study population.

Age (years)	36 ± 13
Sex (male)	260 (53%)
Disease complexity/main cardiac diagnosis	*28 (6%) Simple:*
	15 ASD
	13 VSD
	321 (65%) Moderate:
	52 Aortic coarctation
	35 AVSD
	10 PAPVD
	98 TOF
	22 Ebstein
	19 PS
	18 MVD
	46 BAV/AS
	13 sub/supravalvular AS
	4 Shone syndrome
	4 coronary anomalies
	141 (29%) Complex:
	10 PA
	48 TGA
	29 ccTGA
	9 DORV
	1 DOLV
	14 DILV
	1 DIRV
	16 TA
	3 HLHS
	2 univentricular heart indeterminate type
	7 heterotaxy syndrome
	1 unrepaired AVSD
Physiological stage	A → 38 (8%)
	B → 140 (29%)
	C → 300 (61%)
	D → 12 (2%)
NYHA class	1 → 88 (18%)
	2 → 274 (56%)
	3 → 123 (25%)
	4 → 5 (1%)
Genetic disorders	*47 (10%)*
	25 Down syndrome
	2 Noonan syndrome
	1 Partial 6q trisomy
	1 Duplicate chromosome 8
	1 Ring chromosome Y
	2 Turner syndrome
	1 Myhre syndrome
	2 Williams syndrome
	1 Kartagener syndrome
	2 De George syndrome
	1 Alagille syndrome
	1 Charge syndrome
	1 Pierre Robin syndrome
	1 Moebius syndrome
	1 Kabuki syndrome
	1 Gengival fibromatosis syndrome
	1 Limb-girdle muscular dystrophy
	2 unknown genetic disorder
Comorbidities	*160 (32%)*
	24 obesity
	9 diabetes
	19 dyslipidaemia
	10 hypertension
	6 coronary artery disease
	1 peripheral arterial atherosclerosis
	2 left ventricular non-compaction
	1 abdominal aorta aneurysm
	1 previous myocarditis
	3 thrombotic diathesis
	10 dysventilation syndrome
	25 thyroid dysfunction
	6 renal disease
	10 neurologic/psychiatric disease
	5 extracardiac malformations
	7 haematologic disease
	2 rheumatological disease
	16 gastrointestinal disease
	1 pituitary adenoma
	2 myopathy
Previous thromboembolism	11 embolic stroke
	2 intracardiac thrombosis
	1 pulmonary embolism
	3 deep venous thrombosis
Number of previous cardiac surgeries	1 → 202 (41%)
	2 → 89 (18%)
	3 → 63 (13%)
	≥4 → 9 (2%)

https://doi.org/10.1017/S1047951123000689 Published online by Cambridge University Press

Table 1. (*Continued*)

Cyanosis at rest	20 (4%)
Fontan palliation	31 (6%)
Univentricular physiology	44 (9%)
sRV	99 (20%)
EF (%)	55 ± 9
At least moderate valvular disease	272 (55%)
Previous hospitalisation for HF	144 (29%)
Nt-proBNP (pg/ml)	123 [48–271]
PAH	4 (0.8%)
Chronic oxygen supplementation	7 (1%)
Medications at last visit 329	Betablockers: 169 (34%)
	ACEi/ARB: 240 (49%)
	Antiarrhythmics: 88 (18%)
	Diuretics: 129 (26%)
	Antiplatelets: 50 (10%)
	Anticoagulation: 103 (21%)
PMK	39 (8%)
ICD	16 (3%)/1 (0.2%)

Abbreviations: ACEi=angiotensin converting enzyme inhibitor; ARB=angiotensin 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.

report a history of previous COVID-19 infection, suggesting mildly symptomatic disease.

COVID-19 infection following vaccination

Eighty-two fully vaccinated patients contracted COVID-19 during follow-up: 48 after the primary vaccination cycle at a median of 5.4 [4.3–6.5] months from the last dose and 34 after a median of 1.6 [0.5–2.5] months from the booster dose. Of them, five patients tested positive for COVID-19 twice, before and after COVID-19 vaccination, and one of them with Fontan palliation required hospitalisation in both cases. One patient with Ebstein's disease died from severe COVID-19, 6 months following the booster dose. Symptoms' duration in patients tested positive after vaccination was 5.5 [3–8] days, which was significantly shorter than the symptoms' duration in the group that tested positive before vaccination (9 [2.2–15] days, $p = 0.04$).

Vaccine perception and hesitancy in CHD patients

Data on vaccine attitude were available for 437 (89%) patients: their replies to our vaccine perception questionnaire are summarised in Figure 1. Twenty-nine percent appeared to have concerns regarding vaccine safety before discussing it with their general practitioner or cardiologist, 42% reported fearing potential effects of the vaccine on their cardiac disease, and 43% were at least partially influenced by the discussion with their CHD cardiologist in their decision to undergo COVID-19 vaccination. Sixty-two percent of those vaccinated in situ declared that undergoing vaccination at the CHD centre made them feel safer.

Discussion

After COVID-19 outbreak, healthcare delivery modalities had to be promptly readjusted to meet the new needs of patients worldwide, especially for those who are potentially more vulnerable to the life-threatening effects of COVID-19 infection, like adults with CHD. Those deep changes involved not only a new organisation of the in-hospital care,[12] but also COVID-19 vaccination administration for fragile patients. Between the end of 2020 and the beginning of 2021, in an unprecedented global effort to contain the pandemic, a worldwide imunisation campaign was launched and every country independently started to administer COVID-19 vaccination to the general population. At that time, several scientific statements recommended to prioritise adults with CHD patients in the vaccine allocation strategy.[13–15]

We carried out an observational study with the aim to evaluate the safety profile of COVID-19 vaccines in patients diagnosed with CHD. We previously reported for the first time the early real-life data on COVID-19 vaccination in a small CHD group.[7] However, despite early evidence of success of COVID-19 vaccines in reducing rate of hospitalisation and death, the apparent resolution of the pandemic crisis has led to a more relaxed approach to COVID-19 vaccination in the general population. Nevertheless, very recent news of pandemic resurgence in China with constantly rising numbers of cases[16] should bring back the public and political attention to the importance of protecting fragile populations. In this view, data on long-term results of COVID-19 vaccination in CHD patients are essential to adequately plan the future direction of the vaccination campaign.

Our data provide reassurance of a good mid-term safety profile of the vaccines in the CHD population, confirming our preliminary results.[7] Indeed, post-vaccination adverse events were transient and mild in most cases and included those already mentioned in the summary of product characteristics of these vaccines.[17,18] There was no increased incidence of serious adverse effects in subjects with CHD compared to the general population[19] and the events reported were generally not serious and resolved spontaneously. In line with our results, another observational study carried out in a similar frail population of patients receiving COVID-19 vaccines reported comparable results of adverse events' type, seriousness, and outcome.[20] Post-vaccination acute myopericarditis is a particularly fearsome event in the CHD population, especially in case of presentation with impaired systolic function. However, in our population, it occurred only in one case and was completely resolved after medical treatment. Our data seem to point out a much higher incidence in CHD patients compared to previously reported rate in the available literature, even amongst the highest risk group of young men.[21,22] Nevertheless, this unexpected finding is mostly likely the effect of a random occurrence and no definite conclusions should be drawn from this one event in a limited sample. Further evaluation is needed to ascertain whether the CHD population is at higher risk for post-vaccination myopericarditis. In the meanwhile, a cautious approach with post-vaccination surveillance in CHD patients aimed to detect early symptoms suggestive of myocarditis deserving medical attention may be reasonable. Another worrisome complication is the potential exacerbation of gastrointestinal symptoms in patients on

https://doi.org/10.1017/S1047951123000689 Published online by Cambridge University Press

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

	First vaccine dose	Second vaccine dose	Booster dose
	N = 490	N = 457	N = 301
Adverse events	289 (59%)	248 (51%)	121 (40%)
Symptoms duration range	1–40 days	1–25 days	1–14 days
Local pain	238 (48%)	163 (36%)	81 (27%)
Fever	42 (8%)	67 (14%)	27 (8%)
Headache	42 (8%)	44 (10%)	21(7%)
Myalgia/Arthralgia	72 (15%)	88 (19%)	24 (8%)
Gastrointestinal symptoms	26 (10%)	16 (4%)	8 (3%)
Fatigue/malaise	51 (10%)	56 (12%)	27 (9%)
Diffuse skin rush	4 (0.8%)	2 (0.4%)	0
Others	2 CRP raise	1 late period	1 paresthaesia
	3 dizziness	2 hypotension	2 chills
	1 paresthaesia	1 hypertensive peak	2 palpitations
	1 pharyngodynia	1 dyspnoea	1 dyspnoea
	1 herpes labialis	2 pharyngodynia	1 dizziness
	3 palpitations	1 palpitations	
	2 anosmia	1 chest pain	
	1 chest pain	1 chills	
	3 chills	1 pericarditis	
Medications	42 (9%) paracetamol	46 (10%) paracetamol	16 (5%) paracetamol
	14 corticosteroids	4 NSAIDs	1 NSAIDs
	2 NSAIDs	1 antihistaminics	1 gastrointestinal drugs
	2 gastrointestinal drugs		

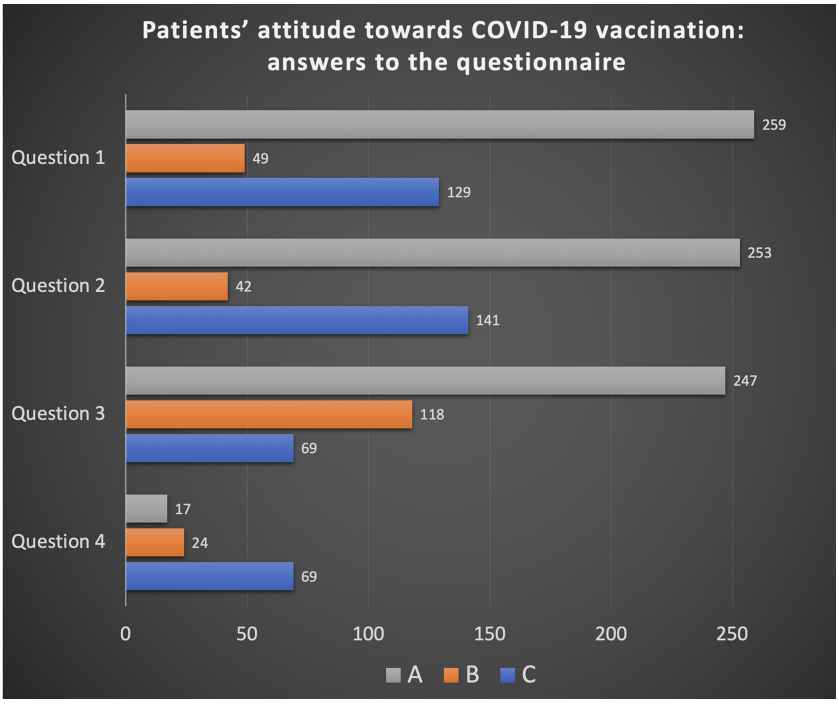

Figure 1. Patients' answers to the vaccine perception questionnaire. Questions are reported in Table 1 of Supplementary material.

https://doi.org/10.1017/S1047951123000689 Published online by Cambridge University Press

chronic diuretic treatment or with Fontan failure. In our series, gastrointestinal disturbs occurred following the first dose, the second, and the booster dose in 10, 4, and 3% of patients, respectively, and were always self-limited. Other rare adverse events were limited in number, required medical treatment on a low proportion of cases and did not seem to cause mid-term complications.

CHD patients developed overall a satisfactory antibody response to COVID-19 vaccines and COVID-19 vaccination was effective in reducing the symptoms duration in case of infection. It is interesting to note that despite multiple risk factors for severe disease in case of viral exposure, 12% of patients with no history of SARS-COV2 infection had positive nucleocapsid antibodies, suggesting a history of asymptomatic or minimally symptomatic prior disease. Vaccine hesitancy was slightly less than what has been reported in other subsets,[23,24] likely due to the effect of the health-related education received since childhood. Patients' answers to our questionnaire highlightened the crucial role of the CHD team to ensure a smooth vaccination acceptance. Nearly all cardiologists are now frequently requested to provide counselling for vaccine hesitancy in patients with cardiac disease. Therefore, educating patients with CHD by pointing out the central role of vaccination during the clinical consultation for the prevention of a potentially life-threatening infection is essential to vaccine acceptance.

Limitations

Our study is limited by sample size, non-randomised design, the lack of cellular immunity, and neutralisation assay testing. Thus, our findings should be considered exploratory since it cannot be excluded that missing clinical data might potentially have influenced our results. Moreover, our population was predominantly composed of subjects with moderate-complex CHD, reflecting the case mix of patients attending a tertiary CHD centre, whereas those with simple defects are more likely followed at local facilities. Furthermore, only 57% of patients attending the clinic in the 4 months following immunisation underwent blood test to quantify IgG titre. Nevertheless, to the best of our knowledge, this is the first study carried out in a real-life context among CHD patients with the aim to describe the current state of COVID-19 vaccination including booster dosage administration, vaccines' safety at a longer follow-up, and protection against COVID-19 infection. The use of our questionnaire is a non-standardised method and could be subject to bias as CHD patients are asked about sentiments prior to the vaccine only after the actual vaccination. However, despite the obvious limits of the questionnaire, it may be a useful tool to explore CHD patients' attitude towards COVID-19 vaccination, allowing to provide the first systematical data on vaccine hesitancy among this population with specific focus on the potential effects of their CHD, addressing safety concerns that these patients might have.

Conclusion

Our study provides the first mid-term real-world evidence of safety and immunogenicity of COVID-19 vaccines in 490 adults with CHD patients, including predominantly individuals with moderate and complex disease. Our data showing lack of a clear trend towards an increased incidence of serious adverse events in adults with CHD patients compared to the general population may be helpful to raise awareness on the safety profile of COVID-19 vaccination and to garner vaccine acceptance in this complex population, though additional reports may be necessary. Moreover, COVID-19 vaccination resulted in a significant reduction of symptoms duration in case of infection among adults with CHD patients, supporting the role of future vaccination campaigns in this peculiar clinical setting, especially in view of possible new pandemic waves.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951123000689

Aknowledgements. We thank Dr Assunta Carandente, lead of the ACHD Unit nursing staff for her tremendous effort in maintaining high-quality standard of care for our complex patients throughout the COVID-19 pandemic; Dr Luigi Atripaldi for his essential contribution in data interpretation; Dr Daniela Costagliola for coordinating the COVID-19 vaccination for patients at risk at AORN dei Colli; Dr Cecilia Spinelli Barrile, Dr Gabriella Piccolo, Dr Nadia Puzone, and Dr Tiziana Varriale for their important work in organizing COVID-19 vaccination in ACHD patients at our centre.

Financial support. This research received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with Helsinki Declaration of 1975, as revised in 2008. Study protocol was approved by the Ethics Committee of Spallanzani Hospital, in agreement with special legislation for prospective studies regarding COVID-19.

References

1. Rafaniello C, Ferrajolo C, Sullo MG, et al. Cardiac events potentially associated to remdesivir: an analysis from the European spontaneous adverse event reporting system. Pharmaceuticals (Basel) 2021; 14: 611. DOI 10.3390/ph14070611.
2. Scavone C, Mascolo A, Rafaniello C, et al. Therapeutic strategies to fight COVID-19: which is the status artis? Br J Pharmacol 2021; 179: 2128–2148. DOI 10.1111/bph.15452.
3. Data from Global Change Data Lab, a non-profit organization based in the United Kingdom. https://ourworldindata.org/covid-vaccinations?country=ITA. Retrieved September 15, 2021.
4. Andrews N, Stowe J, Kirsebom F, et al. Covid-19 vaccine effectiveness against the Omicron (B.1.1.529) variant. N Engl J Med 2022; 386: 1532–1546.
5. Dhama K, Nainu F, Frediansyah A, et al. Global emerging Omicron variant of SARS-CoV-2: impacts, challenges and strategies. J Infect Public Health 2023; 16: 4–14.
6. Broberg CS, Kovacs AH, Sadeghi S, et al. COVID-19 in adults with congenital heart disease. J Am Coll Cardiol 2021; 77: 1644–1655.
7. Fusco F, Scognamiglio G, Merola A, et al. COVID-19 vaccination in adults with congenital heart disease: real-world data from an Italian tertiary centre. Int J Cardiol Congenit Heart Dis 2021; 6: 100266.
8. World Health Organization. Adverse Events Following Immunization (AEFI). Retrieved September 15, 2021, from https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance/health-professionals-info/aefi
9. Italian Medicine Agency. https://www.aifa.gov.it/documents/20142/648668/dir_2010_84_it_0.pdf/b9932078-18b6-011c-8780-1e703514041c
10. Italian Medicine Agency. https://www.aifa.gov.it/documents/20142/834226/Valutazione_studi_infezione_da_SARS-CoV-2_Comitati+Etici_25.05.2020.pdf/caa67824-8e48-eb0d-610c-2557927a7b0b
11. Stout KK, Daniels CJ, Aboulhosn JA, et al. 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. J Am Coll Cardiol 2019; 73: e81–e192. DOI 10.1016/j.jacc.2018.08.1029. Erratum in: J Am Coll Cardiol 2019; 73: 2361–2362.

12. Scognamiglio G, Fusco F, Merola A, Palma M, Correra A, Sarubbi B. Caring for adults with CHD in the era of coronavirus disease 2019 pandemic: early experience in an Italian tertiary centre. Cardiol Young 2020; 30: 1405–1408. DOI 10.1017/S1047951120002085.
13. Driggin E, Maddox TM, Ferdinand KC, et al. ACC health policy statement on cardiovascular disease considerations for COVID-19 vaccine prioritization: a report of the American College of Cardiology solution set oversight committee. J Am Coll Cardiol 2021; 77: 1938–1948.
14. Assenza GE, Castaldi B, Flocco S, et al. COVID-19 vaccine priority access for adults and children with congenital heart disease: a statement of the Italian Society of Pediatric Cardiology. Congenit Heart Dis 2021; 16: 427–431.
15. Sabatino J, Di Salvo G, Calcaterra G, et al. Adult congenital heart disease: special considerations for COVID-19 and vaccine allocation/prioritization. Int J Cardiol Congenit Heart Dis 2021; 4: 100186.
16. European Centre for Disease Prevention and Control. https://www.ecdc.europa.eu/en/news-events/impact-surge-china-covid-19-cases
17. Agenzia Italiana del Farmaco. FAQ Vaccini a mRNA. Retrieved January 02, 2023, from https://www.aifa.gov.it/domande-e-risposte-su-vaccini-mrna
18. European Medicines Agency. https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/safety-covid-19-vaccines
19. Beatty AL, Peyser ND, Butcher XE, et al. Analysis of COVID-19 vaccine type and adverse effects following vaccination. JAMA Netw Open 2021; 4: e2140364. DOI 10.1001/jamanetworkopen.2021.40364.
20. Maniscalco GT, Scavone C, Mascolo A, et al. The safety profile of COVID-19 vaccines in patients diagnosed with multiple sclerosis: a retrospective observational study. J Clin Med 2022; 11: 6855. DOI 10.3390/jcm11226855.
21. Patone M, Mei XW, Handunnetthi L, et al. Risk of myocarditis after sequential doses of COVID-19 vaccine and SARS-CoV-2 infection by age and sex. Circulation 2022; 146: 743–754. DOI 10.1161/CIRCULATIONAHA.122.059970.
22. Oster ME, Shay DK, Su JR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. JAMA 2022; 327: 331–340. DOI 10.1001/jama.2021.24110.
23. Xu R, Shi G, Zheng S, Tung TH, Zhang M. COVID-19 vaccine hesitancy between family decision-makers and non-decision-makers among college teachers. Ann Med 2023; 55: 292–304.
24. Smith LE, Sim J, Amlôt R, et al. Side-effect expectations from COVID-19 vaccination: findings from a nationally representative cross-sectional survey (CoVAccS - wave 2). J Psychosom Res 2021; 152: 110679. DOI 10.1016/j.jpsychores.2021.110679.

https://doi.org/10.1017/S1047951123000689 Published online by Cambridge University Press