Table 1 (*Continued*)

Patient Characteristics	Cardiac resynchronization therapy		p-value
	No (N = 12,278)	Yes (N = 3,289)	
Obesity	8.14%	7.96%	0.856
In-hospital events			
Cardiogenic shock	3.86%	3.81%	0.674
Stroke	1.14%	0.89%	0.368
Acute kidney injury (AKI)	14.31%	15.64%	0.273
Blood transfusion	8.36%	7.10%	0.046
Outcomes			
Mortality	2.77%	2.28%	0.249
Unadjusted OR (95% CI)	Reference	0.79 (0.54-1.12)	0.197
Adjusted OR (95% CI)		0.98 (0.65-1.46)	0.939
Routine Discharge home*	64.78%	66.78%	0.457
Unadjusted OR (95% CI)	Reference	1.09 (0.97-1.22)	0.114
Adjusted OR (95% CI)		1.08 (0.95-1.23)	0.201
30-day readmissions†	29.35%	32.09%	0.108
Unadjusted OR (95% CI)	Reference	1.14 (1.01-1.27)	0.030
Adjusted OR (95% CI)		0.94 (0.81-1.09)	0.414
Length of stay, d	2 (1-6)	2 (1-6)	0.924

Values are median (interquartile range) or n (%), unless otherwise indicated. Categorical variables were compared using Fisher exact test or chi-square test, while continuous variables were compared using Mann-Whitney U test. ORs and 95% CIs were estimated in univariable and multivariable logistic regression models. In multivariable logistic regression models, all variables for patient characteristics were included as covariates.

CI = confidence interval; MI = myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention.

* Includes only patients discharged alive;

† Includes only patients discharged alive before December of each year to allow for a minimum 30 days of follow-up after discharge in the Nationwide Readmissions Database.

international trial[4] showed a similar profile among those poorly responsive to CRT, and confirmed their high HF rehospitalization rate and poor survival. Importantly, such "nonresponders" received little further treatment and were passively managed. Although causes for nonresponse are multiple, nonelectrical solutions may be beneficial and should be considered. Among these, correction of persistent MR among CRT recipients with MitraClip is an effective and safe intervention.

The limitations of our study include lack of echocardiographic data that is, inability to assess MR and left ventricular function. In conclusion, the findings of our study are important and highlight that MitraClip is safe and effective in patients with prior CRT.

Disclosures

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 study.

Agam Bansal, MD
Niraj Varma, MD
Samir R. Kapadia, MD*
Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio

14 June 2021
3 July 2021

1. Upadhyay GA, Chatterjee NA, Kandala J, Friedman DJ, Park MY, Tabtabai SR, Hung J, Singh JP. Assessing mitral regurgitation in the prediction of clinical outcome after cardiac resynchronization therapy. *Heart Rhythm* 2015;12:1201–1208.
2. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, Rajagopal V, Sarembock IJ, Brieke A, Marx SO, Cohen DJ, Weissman NJ, Mack MJ, COAPT Investigators. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med* 2018;379:2307–2318.
3. Kosmidou I, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant BK, Kipperman RM, Boudoulas KD, Redfors B, Shahim B, Zhang Z, Mack MJ, Stone GW. Transcatheter mitral valve repair in patients with and without cardiac resynchronization therapy: the COAPT trial. *Circ Heart Fail* 2020;13:e007293.
4. Varma N, Boehmer J, Bhargava K, Yoo D, Leonelli F, Costanzo M, Saxena A, Sun L, Gold MR, Singh J, Gill J, Auricchio A. Evaluation, management, and outcomes of patients poorly responsive to cardiac resynchronization device therapy. *J Am Coll Cardiol* 2019;74:2588–2603.

https://doi.org/10.1016/j.amjcard.2021.07.006

COVID-19 Vaccine and Myocarditis

The introduction of the various coronavirus disease-2019 (COVID-19) vaccines has resulted in a significant decline in COVID-19 related morbidity and mortality worldwide, and all the approved COVID-19 vaccines have proven to provide benefits that outweigh the potential risks among different age groups.[1–3] Recent reports have raised concerns for myocarditis related to different types of COVID-19 vaccines. However, there are limited data on the characteristics and outcomes of myocarditis in these patients. In this report, we aim to pool the available data to better understand the characteristics and outcomes of the COVID-19 vaccine-related myocarditis.

We conducted a search in the PubMed/Medline database from

Table 1
Characteristics and outcomes of patients with myocarditis related to COVID-19 vaccine

	Age	Sex	Type of vaccine	Dose	Peak cardiac troponin I (ng/mL)	Peak cardiac troponin T (ng/L)	LVEF (%)	Time to resolution (days)
1	25	M	Moderna	2nd	20.4		55%	3
2	21	F	Moderna	2nd	4.4		50%	1
3	17	M	Pfizer-BioNTech	1st	51.37		53%	6
4	28	M	J&J	NA	17.08		50%	2
5	39	M	Pfizer-BioNTech	2nd	11.01		56%	4
6	39	M	Moderna	2nd	13		52%	3
7	24	M	Pfizer-BioNTech	1st	0.37		48%	2
8	19	M	Pfizer-BioNTech	2nd	4.49		50%	3
9	20	M	Pfizer-BioNTech	2nd	0.48		52%	4
10	23	M	Pfizer-BioNTech	2nd	7		50%	2
11	52	M	Moderna	2nd	6.77		54%	4
12	16	M	Pfizer-BioNTech	2nd		1693	61%	6
13	30	M	Pfizer-BioNTech	2nd	12.56		"normal"	Resolved (duration not reported)
14	24	M	Moderna	2nd	18.94		65%	Resolved (duration not reported)
15	39	M	Pfizer-BioNTech	1st		854	"normal"	6

M = male; F = female; LVEF = left ventricular ejection fraction.

inception till June 27, 2021, using the following terms: ("myocarditis" and "covid-19" and "vaccine") with no language restriction. Inclusion criteria were: (1) case reports, case series, and cohort studies; and (2) individuals who developed myocarditis following a COVID-19 vaccine, regardless of the type or dose of the vaccine. The outcomes of interest were peak cardiac troponin I or T levels, left ventricular ejection fraction (LVEF), duration of symptom, and any reported complication.

Our search yielded a total of 15 studies. After applying our inclusion criteria, only 8 studies were included with a total of 15 patients.[4−11] Two of the included studies were case series,[4,6] whereas the rest were case reports.[5,7−11] Fourteen of 15 (93%) of the patients were males. The age range was 17 to 52 years with a mean age of 28 years. Sixty percent of the myocarditis related COVID-19 vaccine cases were associated with the Pfizer-BioNTech vaccine, 33% were associated with the Moderna vaccine, and 7% were associated with the Johnson & Johnson vaccine. All the myocarditis related to the Moderna vaccine (5/5) occurred following the second dose of the vaccine, whereas 6/9 (66.7%) of the myocarditis related to the Pfizer-BioNTech vaccine occurred following the second dose of the vaccine. Peak cardiac troponin I level (ng/mL) was reported in 13/15 patients, and it ranged between 0.37 and 51.37 ng/mL (mean 12.9 ng/mL). Peak troponin T levels were reported in the other 2/15 patients and were 854 ng/L and 1,693 ng/L. Transthoracic echocardiogram in all these patients showed preserved LVEF; exact LVEF value was reported in 13/15 patients with a mean LVEF of 53.5% and a range of 48% to 65%. In the other 2/15 patients, the LVEF was reported as normal with no value. There were no regional wall abnormalities in 14/15 of the patients; 1 patient had subtle apical septal and apical lateral hypokinesis with a LVEF of 52%. All patients recovered within 6 days of their presentation with complications reported (Table 1).

This pooled analysis of the available data shows several important findings. First, myocarditis related to COVID-19 vaccines mostly occurs in young male individuals following the second dose of the vaccine. Second, myocarditis related to COVID vaccines mostly occurs with mRNA vaccines (ie, Pfizer-BioNTech and Moderna COVID-19 vaccines). Third, in all the reported cases of myocarditis related to COVID-19 vaccine, clinical symptoms resolved within 6 days with preservation of the cardiac function. Third, no complications were reported in any of these patients. This analysis shows that myocarditis related to COVID-19 vaccine has an overall fast recovery with no short-term complications.

Disclosures

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.

Husam M. Salah, MD
Jawahar L. Mehta, MD, PhD*
Division of Cardiology, Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas
28 June 2021
6 July 2021

1. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, Brooks N, Smaja M, Mircus G, Pan K, Southern J, Swerdlow DL, Jodar L, Levy Y, Alroy-Preis S. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *Lancet* 2021;397:1819–1829.
2. Lv G, Yuan J, Xiong X, Li M. Mortality rate and characteristics of deaths following COVID-19 vaccination. *Front Med (Lausanne)* 2021;8:670370.
3. Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, Simmons R, Cottrell S, Roberts R, O'Doherty M, Brown K, Cameron C, Stockton D, McMenamin J, Ramsay M. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ* 2021;373:n1088.
4. Mansour J, Short RG, Bhalla S, Woodard PK, Verma A, Robinson X, Raptis DA. Acute myocarditis after a second dose of the mRNA

COVID-19 vaccine: a report of two cases. *Clin Imaging* 2021;78:247–249.
5. Minocha PK, Better D, Singh RK, Hoque T. Recurrence of acute myocarditis temporally associated with receipt of the mRNA COVID-19 vaccine in an adolescent male. *J Pediatr* 2021. [Epub ahead of print].
6. Rosner CM, Genovese L, Tehrani BN, Atkins M, Bakhshi H, Chaudhri S, Damluji AA, Lemos JAd, Desai SS, Emaminia A, Flanagan MC, Khera A, Maghsoudi A, Mekonnen G, Muthukumar A, Saeed IM, Sherwood MW, Sinha SS, O'Connor CM, deFilippi CR. Myocarditis temporally associated with COVID-19 vaccination. *Circulation* 2021. [Epub ahead of print].
7. Muthukumar A, Narasimhan M, Li Q-Z, Mahimainathan L, Hitto I, Fuda F, Batra K, Jiang X, Zhu C, Schoggins J, Cutrell JB, Croft CL, Khera A, Drazner MH, Grodin JL, Greenberg BM, Mammen PPA, Morrison SJ, Lemos JAd. In depth evaluation of a case of presumed myocarditis following the second dose of COVID-19 mRNA vaccine. *Circulation* 2021. [Epub ahead of print].
8. McLean K, Johnson TJ. Myopericarditis in a previously healthy adolescent male following COVID-19 vaccination: a case report. *Acad Emerg Med* 2021. [Epub ahead of print].
9. D'Angelo T, Cattafi A, Carerj ML, Booz C, Ascenti G, Cicero G, Blandino A, Mazziotti S. Myocarditis after SARS-CoV-2 vaccination: a vaccine-induced reaction? *Can J Cardiol* 2021.
10. Albert E, Aurigemma G, Saucedo J, Gerson DS. Myocarditis following COVID-19 vaccination. *Radiol Case Rep* 2021;16:2142–2145.
11. Bautista García J, Peña Ortega P, Bonilla Fernández JA, Cárdenes León A, Ramírez Burgos L, Caballero Dorta E. Acute myocarditis after administration of the BNT162b2 vaccine against COVID-19. *Rev Esp Cardiol (Engl Ed)* 2021. [Epub ahead of print].

https://doi.org/10.1016/j.amjcard.2021.07.009

The Burden of Hospitalizations for Vaccine-Preventable Infections in Heart Transplant Recipients

Over 3,000 heart transplants were performed in the United States in 2020, a 30% increase from 10 years prior.[1] Heart transplant (HT) recipients require life-long immunosuppression, rendering them susceptible to infections. Vaccine-preventable infections (VPI) remain a significant source of morbidity among HT patients. We investigated admissions for VPI and associated healthcare burden in HT recipients.

We queried the National Inpatient Sample database years 2012 to 2014 for patients with and without HT using International Classification of Disease (Ninth edition) Clinical Modification code (ICD-9) V42.1. We then found hospitalization records for VPI by using principal ICD-9 diagnoses for VPI - Herpes Zoster (O53.x), Varicella (O52.x), Meningococcus (O36.x), Influenza (487.x), and Pneumococcal diseases (481, 320.1, 041.2). We excluded patients less than 18 years of age, other organ transplants, hospitalizations with missing death indicators, and elective admissions. The primary outcome was principal diagnosis of VPI. Secondary outcomes were in-hospital death, length of stay, and total hospital charges. Chi-square or Fisher's Exact test was used for categorical variables and Student's *t* test was utilized for continuous variables. Multivariate logistic regression models were generated to identify independent predictors. Elixhauser score was used to quantify each hospitalized patient's total comorbidity burden. Data from the National Inpatient Sample database are publicly available and de-identified; our study was exempt from the institutional review board evaluation. All statistical analyses were conducted with Stata IC 16 (StataCorp, College Station, TX) and accounted for complex survey design and clustering.

The final weighted analysis included 67,528,415 hospitalized patients after exclusions. 505 patients were admitted with VPI and HT; 193,829 patients were admitted with VPI and without HT. Compared with non-transplant recipients, HT patients who were admitted with VPI were younger (56.15 $\pm$ 1.67 vs 66.08 $\pm$ 0.09, p <0.001), less likely female (24.75% vs 55.12%, p <0.001), had a lower overall Elixhauser Comorbidity Score (6.05 $\pm$ 0.79 vs 8.25 $\pm$ 0.05, p <0.001), more likely to be admitted in an urban teaching setting (p <0.001) and at a large hospital (p <0.001). Baseline characteristics are shown in Table 1A. Influenza (7.4 per 1,000) and herpes zoster (5.5 per 1,000) were the most common in HT patients. HT recipients had a higher incidence of admission for VPI compared to the general population (14.6 vs 2.9 per 1,000, p <0.001) (Figure 1A). HT status was a significant contributor in admission for VPI in both the unadjusted and adjusted model (adjusted-OR 5.11; 95% CI 4.19 to 6.23, p <0.001) (Table 1B). There was no significant difference in mortality (p = 0.53), length of stay (p = 0.23), and total hospital charges (p = 0.48) (Figure 1B).

Post-transplant recipients are immunosuppressed, resulting in an attenuated response to vaccines; therefore, timing of post-transplant vaccinations is usually delayed until immunosuppression levels are maintained. As such, pre-transplant vaccinations are critical to establishing immunogenic responses. From 2013 to 2018, Jandhyala and Lewis reported a 58.5% rate of pre-transplant pneumococcal conjugate vaccination and 48.8% rate of pneumococcal polysaccharide vaccination in HT recipients.[2] Blanchard-Rohner et al suggested catch-up immunizations prior to solid organ transplant significantly increased immunity vaccine serological titers, revealing a major window of opportunity during pre-transplant evaluations.[3] Waller et al supported higher rates of influenza and pneumococcal disease in solid organ transplant recipients compared to the general population.[4] Pergam et al reported herpes zoster in 40.0 per 1,000 HT patients in the United States Department of Veteran's Affairs healthcare system, with HT recipients having the highest incidence of herpes zoster infection compared to other types of solid organ transplant recipients.[5] Similar to these previous studies, influenza and herpes zoster were the most encountered VPIs in our cohort of HT patients. Our study is limited by its observational nature, risk of selection biases and residual confounding, and lack of long-term outcomes and possible deaths that took place outside of hospitalizations.

In conclusion, the odds of having a hospital admission for VPI in HT recipients are significantly higher compared to the general population. Influenza and herpes zoster were the most common VPIs in HT recipients. This study emphasizes the importance of optimizing immunization strategies in HT recipients, especially during the pre-transplant period. Further prospective studies are needed to better characterize outcomes in vaccinated HT recipients.