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Letter

Stable Severe Reduction in Ejection Fraction Following COVID-19 mRNA Vaccine: Are They Related?

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Dear Editor,

As the world tries to recover from the coronavirus disease 2019 (COVID-19) pandemic, there is still more to unravel regarding the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and current available vaccines. As the current vaccines have succeeded at curbing the pandemic, there had been a rise in cardiac side effects around the time of vaccine administration.

Inflammatory cardiac disease, or myocarditis, has been recognized in the literature as a rare complication of COVID-19 mRNA vaccines occurring most frequently in the young male population.[1-3] In a population-based study by Goddard et al.,[4] the incidence of myocarditis/pericarditis, in the age group of 5–39 years, was noted to be 1 in 200,000 doses after the 1st dose and 1 in 30,000 doses after 2nd dose. Although no clear mechanism has been identified, potential mechanisms have been proposed in the literature including vaccine induced hyper-immunity or the cross-reactivity of the SARS-CoV-2 spike glycoproteins with myocardial contractile proteins.[5] Most cases are not accompanied by a decrease in cardiac function, and if this occurs, the left ventricular ejection fraction (EF) recovers quickly.[6]

Vaccine-induced takotsubo cardiomyopathy has also been reported in the literature—hypothesized to be due to catecholamine surge following vaccination.[7] In a systematic review by Khalid Ahmed et al.,[8] 10 cases of takotsubo were identified internationally following Pfizer, Moderna, and AstraZeneca vaccines. More than half of the identified cases developed symptoms within approximately 3 days following the first vaccine dose. However, all cases have achieved full recovery within 10.2 days of hospitalization.

There have been almost no reports on profound and stable decrease in cardiac function following mRNA vaccines. We herein report a case series of 3 patients developing severely reduced EF of ≤25% a few weeks following the 2nd dose of the novel Pfizer mRNA COVID-19 vaccine. To our knowledge, there had been no prior mention in the literature of such cases of such severe cardiomyopathy following vaccine administration. Vaccine correlation and potential mechanisms remain to be an enigma.

Table 1. Three cases of coronavirus disease 2019 vaccine related cardiomyopathy with severely reduced ejection fraction

Patient	Symptom onset	Diagnostic studies	GDMT	Outcomes
28-year-old/M	3 weeks after 2nd dose of Pfizer	Troponin: 0.03; BNP: 1,399 CRP: <0.5; ESR: 12 LHC: no significant CAD RHC: PCWP 20; PAP 43/26 (33 mmHg); mild pHTN TTE: severe 4 chamber dilatation; LVEF 15–20%; elevated LVEDP EMB: no inflammatory infiltrates or granulomas	Carvedilol, valsartan, empagliflozin, spironolactone	HeartMate III LVAD placed
22-year-old/M	2 weeks after 2nd dose of Pfizer	Troponin: <0.03; BNP: 2,187; ESR: 10 LHC: no significant CAD RHC: PCWP 13; PAP 42/19 (28 mmHg); mild pHTN TTE: LVEF 15%; moderately reduced RV function; LV, RV, and left atrial dilatation; elevated LVEDP cMRI: moderate to severely dilated LV; no LGA	Sacubitril-valsartan, dapagliflozin, carvedilol, spironolactone	Repeat TTE in 1 month: LVEF 30–33%.
42-year-old/F	1 day after 2nd dose of Pfizer	BNP: 310; ESR:17 LHC: no significant CAD RHC: PCWP 15; PAP 33/16 (23 mmHg); mild pHTN TTE: LVEF 20–25%; LV dilatation; elevated LVEDP cMRI: dilated LV; no LGA	Metoprolol, sacubitril-valsartan, spironolactone	ICD placed Undergoing cardiac transplant evaluation

BNP = brain natriuretic peptide; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; LHC = left heart catheterization; RHC = right heart catheterization; CAD = coronary artery disease; pHTN = pulmonary hypertension; PCWP = pulmonary wedge pressure; PAP = pulmonary artery pressure; LV = left ventricle; RV = right ventricle; TTE = transthoracic echocardiogram; GDMT = guideline-directed medical therapy; LV = left ventricle; LVEF = left ventricular ejection fraction; LVEDP = left ventricular end diastolic pressure; ICD = implantable cardioverter defibrillator; cMRI = cardiac magnetic resonance imaging; LGA = late gadolinium enhancement; EMB = endomyocardial biopsy.

Three patients were identified between January 2021 to August 2021 from hospitalizations or clinic visits (**Table 1**). Each case was evaluated for underlying predisposing conditions, vaccination type, symptoms onset, diagnostic studies, and outcomes. Ages ranged from 22–42 years old. All patients commonly reported clinical symptoms of heart failure including fatigue, orthopnea, paroxysmal nocturnal dyspnea, and peripheral edema within 3 weeks from receiving the 2nd dose of the Pfizer COVID-19 vaccine. Patients had no prior known cardiac history or predisposing conditions. Diagnostic workup including a left heart catheterization showed normal coronaries. Echocardiograms showed significantly reduced left ventricular EF ≤25%. Patients were confirmed to have non-inflammatory cardiomyopathy via endomyocardial biopsy or cardiac magnetic resonance imaging which did not reveal either tissue edema or hyperemia. Since diagnosis, patients were started on guideline directed medical therapy or heart failure while being considered for advanced therapies.

The relationship between the novel mRNA COVID-19 vaccine and cardiomyopathy is an area in need for further investigation. Whether or not the vaccine is a contributing factor remains to be unclear. Yet, the symptoms development following vaccine administration along with the exclusion of other potential etiologies, raises the question of whether they are truly related. Despite the unclear mechanism, management remains to be with guideline-directed medical therapy and advanced therapies, as indicated. EF recovery and improved clinical outcomes can be achieved in some patients.

Even though there had been rare incidences of adverse cardiac events following the novel mRNA COVID vaccines, the benefit of vaccination remains to outweigh the risks. Moreover, in the setting of mass vaccination, some events may be temporally coincidental. The reported potential vaccine complications in the literature, including dilatated cardiomyopathy and inflammatory cardiac disease, can occur independently from vaccination. Therefore, this response is not intended to discourage vaccination—as the efficacy of the vaccines had been evident by flattening of the epidemiological curve and reduction of COVID-related hospitalizations—but rather to pose a topic for further investigation.

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