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REVIEW

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Myocarditis Following COVID-19 Vaccination: A Systematic Review of Case Reports

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Introduction: COVID-19, the infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), often presents with a spectrum of symptoms at varying levels of severity, ranging from asymptomatic patients to those with fatal complications, such as myocarditis. With increased availability of COVID-19 vaccines, the awareness of possible side effects has expanded as reports surface. This study reviewed cases of myocarditis following COVID-19 vaccination and with existing literature on COVID-19 infection-induced myocarditis to compare clinical courses and analyze possible mechanisms of action. **Methods**: A systematic review of literature was conducted to identify published case reports (as of February 3, 2022) pertaining to the development of myocarditis following COVID-19 vaccination with either Pfizer or Moderna for an in-depth analysis. Additional subgroup analyses were conducted based on age, past medical history, vaccine manufacturer, and dose number. **Results**: There were 53 eligible case reports that were included in this study. Patients were mostly male with a median age of 24 years, and the most reported symptom upon presentation was chest pain. Seventy percent of the cases involved the Pfizer vaccine with a majority of myocarditis developing subsequent to second dose. Resolution of symptoms was achieved in all but one patient. Clinical severity, as measured primarily by left ventricular ejection fraction, appeared to be worse among adult patients than pediatric, as well as for patients with comorbidities. **Conclusion**: This study revealed an observable association between COVID-19 vaccines and myocarditis. However, the clinical course and prognosis seem favorable and less prevalent than those conferred from natural infection.

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Abbreviations: COVID-19, Coronavirus Disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; ACE-2, angiotensin converting enzyme 2; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; BNP, B-type Natriuretic Peptide; CK, creatinine kinase; CK-MB, creatinine kinase-myocardial band; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; EKG, Electrocardiogram; ECHO, Echocardiogram; cMRI, cardiovascular magnetic resonance imaging; JBI, Joanna Briggs Institute; PMH, Past medical history; LVEF, Left ventricular ejection fraction; LGE, late gadolinium enhancement; NSAIDs, non-steroidal anti-inflammatory drugs; ACE-i, ACE inhibitors.

Keywords: myocarditis, COVID-19 vaccine, vaccination, myocarditis

Author Contributions: BJB drafted the study design and protocol with aid from RAC, TDG, HZ, and CO. BJB and JMJ completed the study selection process with supervision provided by GAP. BJB completed data extraction and statistical analysis with verification from either RAC, BMB, or DER. BJB, GAP, JMJ, RAC, BMB, JM, DER, TDG, HZ, CO, and NDT contributed to manuscript drafts. GAP served as chief editor in preparation of the manuscript for submission. MJS served as a faculty advisor that oversaw the project, providing input as needed.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a novel infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). A few months following the first documented case in late 2019, a global pandemic was declared by the World Health Organization (WHO) [1]. While the typical clinical presentation of SARS-CoV-2 mimics a lower respiratory tract infection, some individuals develop more severe symptoms [2,3]. Among the complications arising from COVID-19 infection is the development of myocarditis.

Myocarditis is an acute inflammation of the myocardium of the heart arising from several possible etiologies, including viral infections, bacterial infections, and hypersensitivity reactions [4,5]. At onset, characteristic presentation includes dyspnea, fever, and/or chest pain [5]. While the mechanism of action of COVID-19-induced myocarditis is unknown, several hypotheses have been proposed. For example, a recent study found that the spike surface protein of SARS-CoV-2 can bind to the ACE2-anchoring receptor, a receptor associated with cardiovascular, lung, and kidney tissue, causing down-regulation of ACE-2 [6]. ACE-2 is a protein that acts as a cardiac protectant in the development of myocarditis by preventing the pro-inflammatory effects of angiotensin II [6]. An alternative hypothesis of COVID-19 myocarditis suggests a cytokine-mediated etiology due to the observed increase of pro-inflammatory cytokines, such as interleukin (IL)-1, IL-6, and tumor necrosis factor alpha (TNF-a) [7,8].

The breakthrough in vaccine technology towards the end of 2020 led to the FDA (US Food and Drug Administration) approval of two mRNA vaccines for COVID-19: BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna). The vaccines work by introducing mRNA encoding for the spike protein, resulting in an adaptive immune response [9]. Trials demonstrated 94-95% immunization and common mild side effects, such as headache, fatigue, and chills [10,11]. However, since release to the public, more serious side effects have emerged, including myocarditis. According to the CDC, as of February 10, 2022, there have been 1,307 verified reports of myocarditis after COVID-19 vaccination, primarily in people under 30 years old and after receiving either the Pfizer-BioNTech (Pfizer) or Moderna vaccines [12]. This begs the question if the pathogenesis between natural infection and vaccination is similar.

The objective of this study is to perform an in-depth analysis of documented case reports of individuals who developed myocarditis following administration of either the Pfizer or Moderna vaccine. Further, it seeks to compare this clinical course amongst subgroups, as well as against myocarditis associated with natural infection of COVID-19.

METHODS

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist [13].

Eligibility Criteria

This review included studies that (1) were case reports of myocarditis following administration of a mRNA COVID-19 vaccine; (2) dealt with patients that were negative for SARS-CoV-2 at symptom onset; and (3) included a comprehensive explanation of the subsequent clinical course.

Studies were excluded if they were (1) focused on myocarditis following a non-mRNA COVID-19 vaccine, or did not specify the vaccine manufacturer; (2) lacking information on the patient clinical course, such as only discussing autopsy reports or radiographic findings; (3) a case series, defined as consisting of ≥ 2 patients; (4) designed as cohorts, cross-sectional, case-control, or clinical trials; (5) review articles or meta-analyses; or (6) focused on data from vaccine-related adverse event databases.

Information Sources and Search Strategy

A literature search was conducted on PubMed, Cochrane, Web of Science, and Embase to identify case reports of myocarditis following COVID-19 vaccination up to February 3, 2022. Keywords utilized in the databases included “COVID-19 vaccine” or “vaccination” and “myocarditis.”

Selection Process

Eligible articles were imported into Covidence, a systematic review management software, which automatically screened for duplicates [14]. Two authors (BJB and JMJ) independently screened titles and abstracts of the studies, excluding irrelevant studies. Following initial screening, two authors (BJB and JMJ) independently screened full-text articles, examining their adherence to eligibility criteria. Consensus for article inclusion was completed by two authors (BJB and JMJ), with a third author (GAP) serving as an independent mediator.

Data Collection Process and Data Items

Data extraction was completed by the first author (BJB), and subsequently verified for accuracy and completion by another author (RAC, BMB, or DER). The last name of the first author, publication year, country, type and dose of vaccine received, time since vaccination at

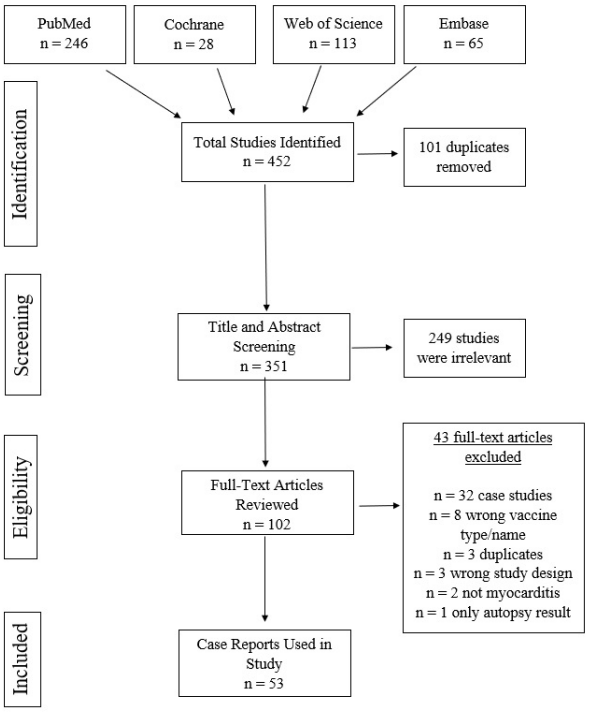

Figure 1. The PRISMA flowchart detailing literature search and selection

presentation, and length of hospitalization were extracted from each eligible case report. Additionally, details on patient demographics, including age, gender, and past medical history (PMH), were obtained. Extracted information pertaining to the clinical course consisted of (1) symptoms at presentation; (2) laboratory values (when provided): troponin, B-type natriuretic peptide (BNP), creatinine kinase (CK), creatine kinase myocardial band (CK-MB), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR); (3) diagnostic imaging: electrocardiogram (EKG), echocardiography (ECHO), and cardiac magnetic resonance imaging (cMRI); (4) medications administered; and (5) whether symptoms resolved.

Risk of Bias in Individual Studies

The Joanna Briggs Institute (JBI) critical appraisal tool for case reports was used to determine the quality of included reports [15]. Each case report was assessed using the eight-question checklist, examining the comprehensiveness of detail inclusion for patient demographics and past medical history, presenting symptoms and severity, description of diagnostic and assessment tests performed, administration of therapeutic interventions or treatments, post-intervention clinical condition assessments, inclusion of any adverse events, and summarized takeaway lessons [15].

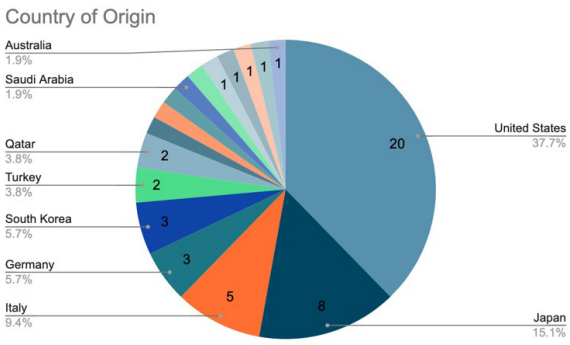

Figure 2. Representation of case report country of origin

Effect Measures and Synthesis Methods

Frequencies of vaccine type and dose number, gender, presenting symptoms, common laboratory and diagnostic imaging findings, medications administered, and whether there was resolution of symptoms were reported. Due to the case reports arising from different facilities, slight variations in reporting were observed. To account for any variations and standardized findings, frequencies were calculated using the number of studies that reported specific parameters as the denominator, with the numerator consisting of studies having the symptom, medication, or laboratory/imaging finding of interest. Time to presentation and length of hospital stay were reported as median and range. Averages for these variables were excluded from analysis due to several outliers that resulted in skewed means. Additional subgroup analyses were conducted by age, PMH, vaccine manufacturer, and vaccine dose number. The same approach for reporting frequencies and medians with ranges was utilized as a comparison for clinical courses, as defined by time since vaccination to presentation, length of hospitalization, left ventricular ejection fraction (LVEF) at presentation, and presence of pericardial effusion.

RESULTS

Study Selection

Four hundred fifty-two articles were identified utilizing key terms in four databases: PubMed (n = 246), Cochrane (n = 28), Web of Science (n = 113), and Embase (n = 65). Duplicates were automatically removed through Covidence; 101 duplicates were excluded from screening, resulting in 351 articles. Two hundred forty-nine studies were deemed irrelevant to this study after the completion of title and abstract screening. The remaining 102 full-text articles were obtained and analyzed for eligibility. Thirty-five studies were excluded for wrong study design, 8 studies were excluded for wrong vaccine type, 3 studies were removed for further duplicity,

Table 1. Summary of Basic Characteristics of Included Studies

Sex (n = 53)	Male	88.7% (n = 47)
	Female	11.3% (n = 6)
Age (n = 53)		Median = 24 years (Range: 14 – 80 years)
Time to Pt (n = 53)		Median = 3 days (Range: 1 – 90 days)
Vaccine (n = 53)	Pfizer	69.8% (n = 37)
	1st dose	13.2% (n = 7)
	2nd dose	54.7% (n = 29)
	Unspecified	1.9% (n = 1)
	Moderna	30.2% (n = 16)
	1st dose	5.7% (n = 3)
	2nd dose	24.5% (n = 13)

2 studies were excluded due to study focuses outside of myocarditis, and study was excluded for insufficient case information, resulting in a total of 49 sources excluded and 53 case reports deemed eligible for inclusion in this study (Figure 1).

Study Characteristics

All 53 included studies were published from June 1, 2021 to February 2, 2022 [16-68]. Case reports originated from 17 different countries with the US accounting for 20, Japan for 8, and Italy for 5 (Figure 2).

Of the 53 cases, 47 patients were male (88.7%). The median age was 24 years (range: 14-80 years), and median time from vaccination to presentation was 3 days (range: 1-90 days). The Pfizer vaccine was received by 37 patients (69.8%), while the Moderna accounted for 16 (30.2%). Of the 52 studies that reported dose number, 42 (80.8%) occurred after the second dose (Table 1).

Past medical history was recorded in 52 of the studies; 35 (67.3%) individuals reported no previous conditions or diseases, 10 (19.2%) individuals had prior cardiovascular-related conditions or diseases, and 7 (13.5%) individuals indicated that they had prior medical history unrelated to cardiovascular conditions or diseases. Of the conditions unrelated to cardiovascular etiology, the most frequently reported chronic conditions were asthma (n = 4), hyperlipidemia (n = 3), and type 2 diabetes (n = 2) (Figure 3).

Risk of Bias in Included Studies

One case report only received "yes" to five of the eight questions on the JBI critical appraisal tool, whereas the remaining 52 studies had six or more [58]. The average risk bias assessment score for the included case reports for this study was 6.8/8.

Results of Syntheses

Presentation: All 53 case reports described symptoms at presentation, with chest pain being the most frequently reported at 90.6% (n = 48). Fever and dyspnea were the next most common symptoms at 32.1% (n = 17) and 24.5% (n = 13), respectively (Figure 4).

Laboratory Tests and Imaging Findings: Troponin levels were measured in each of the 53 reports, with elevated ranges present in all but one (98.1%). Elevations in other cardiac biomarkers were also frequently seen—BNP was elevated 69.6% of the time, while the CK and CK-MB were elevated 94.1% and 93.8%, respectively. Inflammatory markers, CRP and ESR, were also frequently elevated at 86.4% and 83.3%, respectively (Table 2).

An EKG was performed in all but one case, with normal findings reported in 8 patients (15.4%). Among abnormal findings were ST elevations in 35 (67.3%), sinus tachycardia in 9 (17.3%), and non-specific T-wave abnormalities in 8 (15.4%) (Table 2).

An ECHO was performed in 50 of 53 patients. A preserved LVEF (≥55%) was noted in 28 (56%) of the cases. In addition to the reduced LVEF seen in the other 22 (44%), wall hypokinesis and pericardial effusion were reported in 17 (34%) and 11 (22%), respectively (Table 2).

cMRI was performed in 42 of 53 patients, with abnormal results present for each patient. Abnormal findings included a "suggestive" or "positive" finding for myocarditis in 2 (4.8%) patients, while 40 (95.2%) showed late gadolinium enhancement (LGE) and 26 (61.9%) showed edema (Table 2).

Clinical course: The length of hospital stay was reported in 40 of the 53 cases, with a median of 5.5 days (range: 2-21 days). Resolution of symptoms was reported in 52 cases, with only one patient having ongoing heart

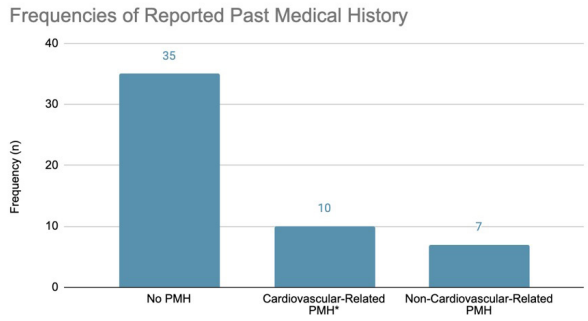

Figure 3. Graphical representation of frequencies in reported past medical conditions or diseases

*Cardiovascular-related conditions include: hypertension (n=4), heart failure (n=2), coronary artery disease (n=2), history of previous myocarditis (n=2), arrhythmogenic left ventricular cardiomyopathy (n=1), Kawasaki Disease (n=1), and mitral valve prolapse (n=1).

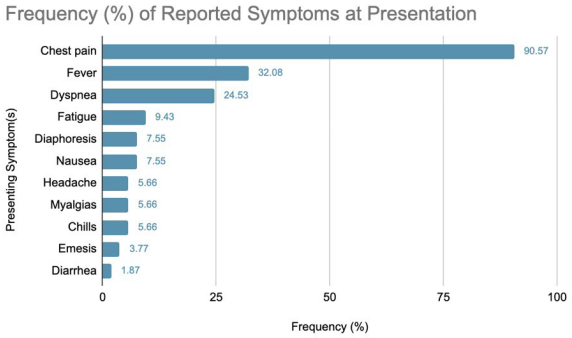

Figure 4. Graphical representation of frequency of reported presenting symptom(s)

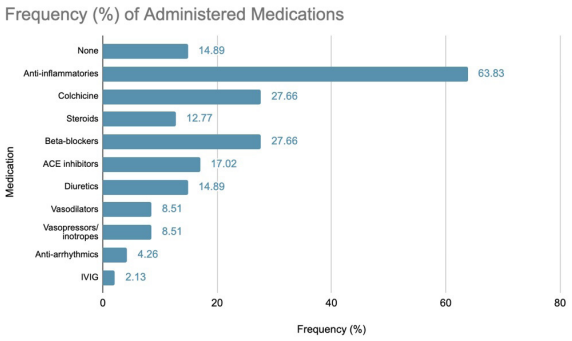

Figure 5. Graphical representation of frequencies (%) for medications administered

failure [16]. Of the 22 patients with reduced LVEF, only three did not have resolution [16,19,37].

Therapeutic interventions and/or medications administered during hospitalization stays were provided for 47 cases. Seven (14.9%) cases reported spontaneous resolution without medical intervention. The most commonly prescribed medications were anti-inflammatories (NSAIDs, aspirin, acetaminophen) at 63.8%. Additionally, colchicine and beta-blockers were used 27.7% of the time, followed by ACE-inhibitors and diuretics at 17% and 14.9%, respectively (Figure 5).

Subgroup Analyses

Age: Cases were classified into subgroups based on patient age, such that two groups were comprised of 1) individuals aged 17 years old or younger (pediatric group, n = 7) and 2) those aged 18 years or older (adult group, n = 46). For both groups, the median time from vaccination to presentation was 3 days, but the median range of hospitalization length in the pediatrics group (6 days) was 1 day longer than the adult group (5 days). Diagnostic findings reported for 50 patients (pediatric, n = 7; adult, n = 43) demonstrated a reduced LVEF finding in one pediatric patient (14%) versus 21 adult patients (48.8%). Furthermore, pericardial effusion findings were only observed in 12 (27.9%) of adult patients and none of the pediatric patients (Table 3).

PMH: Past medical history was broken down into three groups: none reported (n = 35), significant for a cardiovascular condition (n = 10), and significant for another (non-cardiovascular-related) disease (n = 7). The median time from vaccination to presentation was 3 days for all three groups. The median length of hospitalization was 6 days for those with a pre-existing cardiovascular condition, compared with 5 days for the other two groups. ECHO findings showed a reduced LVEF in 33.3% (11/33) of those with no PMH, 66.7% (6/9) in those with a cardiovascular condition, and 57.1% (4/7) for other PMH. The rates of pericardial effusion for the three groups were 24.2% (8/33), 11.1% (1/9), and 28.6% (2/7), respectively. Furthermore, the three patients in this study that did not experience resolution of their reduced LVEF had a significant PMH, with one having coronary artery disease (CAD), another having arrhythmogenic left ventricular cardiomyopathy (ALVC), and the last having glioblastoma multiforme [16,19,37] (Table 3).

Vaccine Type: The median time from vaccination to presentation was 3 days for both the Moderna and Pfizer vaccines. The median length of hospitalization was 6 days for the Pfizer vaccine versus 5 days for the Moderna vaccine. ECHO findings for the Pfizer group (n = 35) demonstrated reduced LVEF in 13 (37.1%) and pericardial effusion in 9 (25.7%), compared to 8 (53.3%) and 3 (20%), for the Moderna group (n = 15), respectively (Table 3).

Vaccine Dose: The median time from vaccination to presentation was 4 days for those receiving their

Table 2. Frequencies of Lab/Imaging Findings

Common Laboratory Tests and Diagnostic Imaging Findings		Frequency of Elevation (Labs)/Finding (Imaging) in % (n)
Labs	Troponin (n = 53)	98.1% (52)
	BNP (n = 23)	69.6% (16)
	CK (n = 17)	94.1% (16)
	CK-MB (n = 16)	93.8% (15)
	CRP (n = 44)	86.4% (38)
	ESR (n = 18)	83.3% (15)
EKG (n = 52)	Normal	15.4% (8)
	ST elevation	67.3% (35)
	PR depression	11.5% (6)
	Sinus tachycardia	17.3% (9)
	Non-specific ST-segment abnormalities	3.8% (2)
	Non-specific T-wave abnormalities	15.4% (8)
	Right Bundle Branch Block (RBBB)	5.8% (3)
	ST depression	5.8% (3)
ECHO (n = 50)	Preserved LVEF (≥55%)	56% (28)
	Reduced LVEF (<55%)	44% (22)
	Wall hypokinesis	34% (17)
	Pericardial effusion	22% (11)
cMRI (n = 42)	LGE	95.2% (40)
	Edema	61.9% (26)
	Suggestive/positive for myocarditis	4.8% (2)

first dose, compared with 3 days for those receiving the second dose. The median length of hospitalization was 2 days longer for the second-dose recipients at 6 days than first-dose recipients (at 4 days). ECHO findings for first-dose recipients (n = 10) showed 5 (50%) with a reduced LVEF and 1 (10%) with pericardial effusion, compared to 15 (38.5%) and 10 (25.6%), respectively, for the second-dose recipients (n = 39) (Table 3).

Reporting Biases

Data extracted from each case varied slightly due to the range of study settings observed among reports. The resultant reduction in available data points may have contributed to potentially skewed results, particularly in regard to the frequencies used in the subgroup analysis.

DISCUSSION

Upon completion of analyses of the 53 case reports detailing the clinical discourse of myocarditis following COVID-19 vaccination, several observations can be drawn regarding patients' clinical outcomes. The median time between vaccination and presentation to the hospital was 3 days. Cases occurred primarily in younger adult males and after the second dose of vaccine. The Pfizer vaccine accounted for roughly 70% of all cases.

Diagnosis of myocarditis was aided by the presence of elevated serum cardiac biomarkers, such as troponin, BNP, CK, and CK-MB, as well as diagnostic imaging findings from EKG, ECHO, and cMRI [5]. Abnormal EKGs were seen 84.6% of the time with ST elevations and sinus tachycardia among the two most common abnormalities. ECHO imaging demonstrated reduced LVEF among 44% of patients, as well as additional abnormal findings, such as wall hypokinesis and pericardial effusion in 34% and 11% of patients, respectively. LVEF is the central measure of left ventricular systolic function and serves as a useful indicator of heart function [69]. Pericardial effusion, or fluid accumulation in the peritoneal layer surrounding the heart can also provide insight into disease severity as it often precedes cardiac tamponade, a life-threatening complication of myocarditis [70]. Wall hypokinesis, or decreased heart wall motion, is an adjuvant indicator for myocarditis often seen alongside LVEF findings that may indicate a worse prognosis than the presence of reduced LVEF alone [71]. cMRI is a sensitive, non-invasive imaging procedure often utilized to aid the diagnosis of myocarditis through the identification

Table 3. Subgroup Analyses Based on Age, Past Medical History, Type of Vaccine, and Vaccine Doses

		Time to Presentation		Length of Hospitalization		ECHO Findings		
Subgroup		N	Median (Range)	N	Median (Range)	N	Reduced LVEF	Pericardial Effusion
Age	Peds	7	3 days (1-4 days)	7	6 days (2-7 days)	7	14.3% (n = 1)	0
	Adults	46	3 days (1-90 days)	33	5 days (2-21 days)	43	48.8% (n = 21)	27.9% (n = 12)
PMH	None	35	3 days (1-26 days)	27	5 days (2-10 days)	33	33.3% (n = 11)	24.2% (n = 8)
	Cardiac	10	3 days (1-90 days)	8	6 days (3-14 days)	9	66.7% (n = 6)	11.1% (n = 1)
	Other	7	3 days (1-10 days)	5	5 days (2-21 days)	7	57.1% (n = 4)	28.6% (n = 2)
Vaccine	Pfizer	37	3 days (1-90 days)	29	6 days (2-12 days)	35	37.1% (n = 13)	25.7% (n = 9)
	Moderna	16	3 days (1-26 days)	11	5 days (3-21 days)	15	53.3% (n = 8)	20% (n = 3)
Dose	1st Dose	10	4 days (3-12 days)	6	4 days (2-12 days)	10	50% (n = 5)	10% (n = 1)
	2nd Dose	42	3 days (1-90 days)	33	6 days (2-21 days)	39	38.5% (n = 15)	25.6% (n = 10)

of characteristic findings for myocarditis, such as late gadolinium enhancement (LGE) [5]. LGE refers to the differing uptake and washout patterns of the administered gadolinium-based contrast agents from the myocardial extracellular space between normal and diseased myocardial tissue, alluding to an ongoing cardiac injury [72].

Across each subgroup, the time from vaccination to presentation and length of hospitalization were fairly consistent. Variations were noted in the ECHO findings of reduced LVEF and presence of pericardial effusion, two measures that could suggest clinical severity. Specifically, reduced LVEF and the presence of pericardial effusion were seen more frequently in adults than pediatrics. While our pediatric sample size was small, a case series of 15 children with a median age of 15 years found a reduced LVEF in only 3 patients and no pericardial effusion in any, yielding similar frequencies to what we obtained in this study [73]. Furthermore, the frequencies of reduced LVEF were higher in patients with a significant PMH of any chronic illness in comparison to healthy patients. This was particularly pronounced in those with a cardiovascular-related PMH, and these patients also accounted for two of the three cases in which LVEF did not resolve, with one having ongoing heart failure.

A recent systematic review of case reports and case series with 227 patients with myocarditis following mRNA COVID-19 vaccines achieved similar results to the current study [74]. Patients in this study had a median age of 21, were mostly males (92.1%), presenting predominantly after the second dose of the Pfizer vaccine with chest pain (96.1%) and fever (38.2%) [74]. Reported results included both a median time to presentation since vaccination and length of hospitalization of 3 days [74]. Elevations were also frequently seen in troponins (99.5%), CK-MB (100%), BNP (78.3%), CRP (90.1%), and ESR (60.5%) [74]. However, they defined reduced LVEF as below 50%, as opposed to our 55%, so this was only seen in 18.2% of their cases [74].

Although conclusions regarding mechanism of action cannot be definitively drawn, comparisons in the clinical discourses of vaccine-induced myocarditis can be made to myocarditis resulting from natural infection. For example, a study consisting of 718,365 COVID-19 patients found that patients presenting with primary COVID-19 infection had a 5% chance of developing myocarditis/pericarditis [75]. Among the approximate 36,000 individuals susceptible to myocardial/pericardial involvement, there exists an increased risk of developing an adverse outcome, including death [75]. Conversely, only 1,307 verified reports of myocarditis have been connected to COVID-19 mRNA vaccination [12]. Furthermore, a systematic review examining the frequency of diagnostic imaging findings and clinical outcomes among 215 COVID-19 patients that developed myocarditis provides contextual comparison against patients who developed vaccine-induced myocarditis [76]. While patients with

naturally-induced myocarditis demonstrated lower rates of reduced LVEF (31.4%), as compared to patients with vaccine-induced myocarditis (44%), naturally infected patients had increased occurrences of complications, including acute respiratory distress syndrome (66.4%) and cardiogenic shock (14%), with an overall survival rate of 64.7% [76]. Similarly, a review of 38 reports detailing COVID-19 associated myocarditis noted that 37% of patients required treatment for heart failure during hospitalization, and 15% of this patient population were eventually discharged with persistently reduced LVEF [77]. However, in our study, only 6% of patients had a persistently reduced LVEF.

While the sample size in this study, in addition to alternative citations, is relatively small and has decreased generalizability, this can be attributed to the novel nature of this disease course and proposed pathogenesis. Further, due to the rapid global prevalence of this disease, case reports were compiled from various facilities with differing laboratory and imaging capabilities.

Nonetheless, the amalgamation of the information reported on the clinical discourse observed between vaccine-induced myocarditis and naturally-induced myocarditis suggests a poorer prognosis among myocarditis patients due to natural infection. These findings contribute to the cost-benefit analysis favoring COVID-19 vaccination for disease prevention and mitigation.

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