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# Clinical Cardiovascular Adverse Events Reported Post-COVID-19 Vaccination: Are They a Real Risk?

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**Abstract:** Given the urgent need to control the spread of the novel COVID-19 virus, 13 vaccines have been approved for emergency use before completing all 3 phases of the clinical trials. Thereby a careful monitor of the adverse effects postvaccination is essential. We searched through PubMed and other reporting systems like VAERS for the reported cardiovascular adverse events post-COVID-19 vaccination. Through our review, we determined that the incidence of all the reported cardiovascular events is very rare. Additionally, the vaccine was initially given to the elderly and high-risk populations in which cardiovascular events such as myocardial infarction and arrhythmias are already more prevalent, while other cardiovascular events such as myocarditis or vaccine-induced thrombotic thrombocytopenia were more common in younger populations. Moreover, a direct causal relationship, if any, between vaccination and adverse events is yet to be fully elucidated. Thus, at this time point, the benefits of vaccination far outweigh the risk. (Curr Probl Cardiol 2022;47:101077.)

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Curr Probl Cardiol 2022;47:101077  
0146-2806/\$ – see front matter  
<https://doi.org/10.1016/j.cpcardiol.2021.101077>

## Introduction

**I**n December 2019, coronavirus disease 2019 (COVID-19) emerged in Wuhan, China. The virus spread globally and infected millions of individuals worldwide. The management of patients infected with this novel virus was challenging, particularly in the early days of the pandemic. Over a year, researchers faced significant challenges in discovering therapies and vaccines for this novel virus. Given the urgent need to control the spread of the virus, 13 vaccines have been approved for emergency use in many countries before completing all 3 phases of the clinical trials, which prompted investigators to carefully monitor the adverse effects postvaccination.<sup>1</sup>

Adverse effects such as fatigue, headaches, and local injection site reaction have been reported after receiving COVID-19 vaccines; however, rare serious adverse events were also recorded.<sup>2,3</sup> Multiple studies reported cardiovascular complications in hospitalized patients with COVID-19 infection.<sup>4,5</sup> Recently few reports described rare cardiovascular adverse events post-COVID-19 vaccination.<sup>6</sup> Although some of these reported adverse events are serious, the benefits of vaccination outweighed the risks.<sup>7,8</sup> There are also reports of similar rare complications following vaccination with other vaccines such as smallpox and influenza.<sup>9</sup> The relation between vaccination and these rare complications is still ambiguous. However, the occurrence of these rare events postvaccination with the absence of any other obvious cause may suggest that the vaccine can be a precipitant factor. It is essential to report these adverse events along with long-term follow-up of patients with these complications. In this review, we describe the cardiovascular complications that were reported post-COVID-19 vaccination, such as myocarditis, pericarditis, thrombotic events in addition to other rare, reported cases of hypertension, acute coronary syndrome, stress cardiomyopathy, arrhythmias and cardiac arrest.

## COVID-19 Vaccine-Related Myocarditis and Pericarditis

COVID-19 mRNA vaccinations set a precedent in the field of virology with their rapid development and demonstration of safety and effectiveness.<sup>3,2</sup> The 2 mRNA vaccines granted emergency use authorization by The Food and Drug Administration (FDA) in the US include Pfizer (BNT162b2, Pfizer-BioNTech; Philadelphia, PA, USA) and Moderna (mRNA-1273, ModernaTX, Inc; Cambridge, MA, USA) vaccines.

The Janssen vaccine (JNJ-78436735, Johnson & Johnson; New Brunswick, NJ, USA), which is a viral vector vaccine, was also granted emergency use authorization later. Within weeks of increasing reports of myocarditis and pericarditis following COVID-19 vaccination, the Center for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) convened to examine the risks and benefits. On June 23, 2021, the committee determined that there was likely an association between COVID-19 vaccines and myocarditis and pericarditis though the benefits still far outweighed the risks.<sup>7</sup> When viewed historically, myocarditis and pericarditis after vaccination is not a new phenomenon. There are reported cases as early as 1957 following vaccinations for smallpox, hepatitis B, and even influenza.<sup>9</sup> However, the incidence of these cases is rare with only smallpox vaccination having a strong correlation with myocarditis and pericarditis.<sup>10</sup>

Myocarditis is idiopathic in about 50% of cases.<sup>11</sup> In patients with an identifiable cause, the most common cause is viral. Other causes can include granulomatous inflammatory diseases, polymyositis and dermatomyositis, and collagen vascular diseases.<sup>12</sup> Myocarditis is more common in younger adults and appears to affect both genders equally.<sup>13</sup> The pathophysiology is believed to be largely immune-mediated. It is proposed that the microbial agent gains entry through either the gastrointestinal or respiratory tracts and binds to specific receptors in the myocardium leading to cell lysis and subsequent immune dysfunction with molecular mimicry playing a large role. The variable clinical presentation of myocarditis makes it difficult to estimate the incidence, though it is thought to be 10-20 per 100,000 cases per year with 1.5 million cases worldwide.<sup>14</sup> Pericarditis has a similar etiology to myocarditis.<sup>15</sup>

As of September 11, 2021, 379 million COVID-19 vaccine doses had been administered in the US. Of those, 216 million were Pfizer, 148 million were Moderna, and 15 million were Janssen.<sup>16</sup> The Vaccine Adverse Event System (VAERS) is a safety signal detection system that reports adverse events to the CDC and FDA for post-licensure safety monitoring. Although this system is useful in data analysis and hypothesis generation, it is important to note that this system is subject to reporting bias and most VAERS events cannot be directly linked to vaccinations.<sup>17</sup> Between December 29, 2020, and September 10, 2021, a total of 1670 cases of myocarditis (1108 with Pfizer, 519 with Moderna, 39 with Janssen, 4 unknown) and 1115 cases of pericarditis (662 with Pfizer, 388 with Moderna, 60 with Janssen, 5 unknown) were reported in VAERS (Table 1).<sup>18</sup> In considering the proportion of the doses given from each manufacturer to the number of reports of myocarditis and pericarditis, it is apparent

**TABLE 1.** The common cardiovascular complications reported in the Vaccine Adverse Event System (VAERS) as of September 10, 2021 in the United States/territories/unknown

Specific adverse event	Total number of events	Pfizer/BioNTech	Moderna	Janssen	Unknown
Myocarditis	1670	1108	519	39	4
Pericarditis	1115	662	338	60	5
Thrombosis	3066	1353	964	740	9
Pulmonary embolism	2666	1096	1079	466	25
DVT	1960	780	749	418	13
CVST	168	57	58	52	1
Mesenteric vein thrombosis	48	18	22	8	
Pelvic venous thrombosis	30	17	6	7	
Splenic vein thrombosis	20	6	10	4	
Hepatic vein thrombosis	11	4	3	4	
Thrombocytopenia	653	325	221	104	4
Hypertension	5272	2546	2227	490	9
Hypertensive crisis	72	32	34	5	1
Hypertension urgency	45	26	14	5	
Malignant hypertension	5	4	1		
Myocardial infarction	1125	561	459	102	3
Acute myocardial infarction	737	397	293	44	3
Angina pectoris	594	363	175	56	
Stress cardiomyopathy	39	21	16	2	
Palpitation	11,252	5704	4633	897	18
Arrhythmia	690	385	265	39	1
Tachycardia	4908	2489	2114	294	11
Atrial fibrillation	1830	899	806	123	2
Extrasystole	330	180	136	14	
Sinus tachycardia	411	221	151	38	1
Supraventricular tachycardia	325	168	141	16	
Bradycardia	549	275	201	71	2
Cardiac arrest	830	416	334	72	8
Death	6181	2885	2739	534	23

CVST, cerebral venous sinus thrombosis; DVT, deep venous thrombosis.

The total number of vaccines doses is 379 million doses.

that there was no manufacturer with a considerably increased number of myocarditis or pericarditis cases. This was also the case for the Janssen vaccine suggesting that the mRNA vaccine platform likely does not increase the probability of myocarditis or pericarditis. In both myocarditis and pericarditis, about three-fourths of reports were after the second mRNA dose.<sup>18</sup> The median age for myocarditis was approximately 24 in both males and females, while the median age for pericarditis was approximately 24 in males and 54 in females.<sup>18</sup> There was a total of 1177 reports of myocarditis in males and 330 reports in females. There were 651 reports of pericarditis in males and 340 reports in females.<sup>18</sup> Thus, there is a male predominance in both myocarditis and pericarditis reports, though the difference was less stark with pericarditis. This male

predominance may be rationalized by sex hormone differences. Notably, testosterone plays a role in the inhibition of anti-inflammatory cells and commitment to Th1 type immune response,<sup>19-21</sup> while estrogen has an inhibitory effect on proinflammatory T cells.<sup>22</sup> This may also explain the greater incidence of pericarditis after COVID-19 vaccination in postmenopausal females. However, this is not seen with myocarditis.<sup>18</sup>

Several reports of myocarditis or pericarditis after COVID-19 vaccination have been published.<sup>23-34</sup> The common presentation was chest pain, followed by fever, and rarely headache, cough, and dyspnea. Symptom onset was about 2-3 days after vaccination, commonly after the second dose. All patients tested negative for COVID-19 upon presentation. Patients had elevated troponin and C-reactive protein (CRP), and electrocardiograph (ECG) showed ST elevations in most reports. Most cases required hospitalization for up to 4 days but were still considered mild.<sup>23-34</sup>

In reports of post-COVID-19 vaccination myocarditis, there have been 2 cases that included cardiac biopsies, which lacked the expected myocardial infiltration.<sup>32,34</sup> PCR testing of cardiac tissue for SARS-CoV-19 virus was also negative.<sup>32,34</sup> Though caution should be taken when hypothesizing based on only 2 cases, this may suggest there is a different mechanism leading to myocardial injury than the usual microbial and lymphocyte infiltration of myocardial tissue.

In a case report, it was shown that the IgG and IgM antibody levels against SARS-CoV-2 spike protein were not different in a patient with myocarditis than in individuals without myocarditis post-COVID-19 vaccination.<sup>25</sup> This argues against a hyperimmune response. Molecular mimicry has also been hypothesized as a potential mechanism. Antibodies against SARS-CoV-2 spike proteins have been shown to cross react with similar human protein sequences including  $\alpha$ -myosin.<sup>35</sup> However, reports typically lack severe autoimmune reactions. COVID-19 infection has been associated with an increased incidence of myocarditis and pericarditis,<sup>5</sup> which would raise the question of whether breakthrough infections could explain postvaccination myocarditis and pericarditis. However, in most reports, patients tested negative for COVID-19.<sup>23-34</sup> Innate response to mRNA vaccine products such as the lipid nanoparticles or other adjuvants is also unlikely as these have been shown to not result in an inflammatory or immune response.<sup>3,2</sup> In addition, cases of myocarditis and pericarditis have also been reported in the Janssen vaccine as well, which is not an mRNA-based vaccine.<sup>18</sup>

In patients presenting with chest pain after COVID-19 vaccination, management should include ECG, troponins, and inflammatory markers.<sup>12</sup> Hospitalization may be required for patients with signs of

myocardial injury, arrhythmia, or hemodynamic instability. Supportive care along with nonsteroidal anti-inflammatory drugs should be given, though published cases have used steroids and colchicine as well.<sup>26,29</sup> Strenuous physical activity should also be limited until resolution. The CDC currently recommends delaying the second dose when applicable if myocarditis or pericarditis occurs following the first dose, though the CDC still recommends considering obtaining the second dose following resolution.<sup>36</sup>

Although there has been a considerable amount of attention and media discussions on post-COVID vaccination myocarditis and pericarditis, the number of cases is relatively very small considering the number of vaccine doses administered. COVID-19 infection itself yields a considerable risk of hospitalization, death, myocarditis, and pericarditis, which is much greater than that related to COVID-19 vaccination.<sup>7</sup> Thus, the risk-benefit discussion overwhelmingly favors vaccination. COVID-19 vaccination not only decreases hospitalization due to COVID-19 complications and death, but it also decreases COVID-19 complications including myocarditis and pericarditis.<sup>37,38</sup>

## **COVID-19 Vaccine-Induced Thrombotic Thrombocytopenia**

Within a few weeks of initiating public vaccination efforts, several rare cases of vaccine-induced thrombotic thrombocytopenia (VITT) have been reported after receiving COVID-19 vaccines, especially following the adenoviral vector AstraZeneca and Janssen vaccines. These rare cases of VITT have a significant impact on stumbling the global vaccination program progression.<sup>39,40</sup> Such reports led to a temporary pause of Janssen vaccine use from April 13-23, 2021. On April 23, 2021, the CDC's ACIP reaffirmed its recommendation for Janssen vaccine use in all persons  $\geq 18$  years old. On April 30, the ACIP added a warning of rare thrombotic events and recommended that younger women  $< 50$  years old should be aware of such rare complications.<sup>41</sup> Similar conclusions were made for the AstraZeneca vaccine, which included younger persons  $< 50$  years old have a higher incidence than those  $> 50$  years old (18 per million doses vs 12 per million doses).<sup>42</sup> The median onset of symptoms after AstraZeneca and Janssen vaccines are 10 (5-24) and 8 (6-15) days, respectively.<sup>43</sup>

As of September 10, 2021, among 379 million COVID-19 vaccine doses in the US, a total of 3066 cases of unspecified thrombosis, 2666 cases of pulmonary embolism, 1960 cases of DVT, 168 cases of cerebral

**TABLE 2.** The common cardiovascular complication reported according to the case series drug analysis print published by United Kingdom (UK) government for AstraZeneca vaccine

Specific adverse event	Total number of events	Fatal events
Myocarditis	105	1
Pericarditis	162	0
Thrombosis	1712	33
Pulmonary embolism	1582	100
DVT	1173	9
CVST	207	22
Mesenteric vein thrombosis	20	0
Pelvic venous thrombosis	22	1
Splenic vein thrombosis	10	0
Hepatic vein thrombosis	16	0
Thrombocytopenia	868	6
Hypertension	941	0
Hypertensive crisis	14	0
Hypertension urgency	4	0
Malignant hypertension	4	0
Myocardial infarction	386	51
Acute myocardial infarction	79	13
Angina pectoris	219	0
Stress cardiomyopathy	5	0
Palpitation	5157	1
Arrhythmia	134	3
Tachycardia	1242	0
Atrial fibrillation	311	0
Extrasystole	142	0
Sinus tachycardia	69	1
Supraventricular tachycardia	41	0
Bradycardia	78	0
Cardiac arrest	167	35
Death	301	301

CVST, cerebral venous sinus thrombosis; DVT, deep venous thrombosis.

venous sinus thrombosis (CVST), and 653 cases of thrombocytopenia were reported in VAERS (Table 1).<sup>18</sup> As of September 10, 2021, the Case Series Drug Analysis Print published by the United Kingdom (UK) government for the AstraZeneca vaccine, reported a total of 1712 unspecified thrombotic events, 1173 events of DVT, 1582 events of pulmonary embolism, 207 events of CVST, and 868 events of thrombocytopenia (Table 2).<sup>44</sup> Again, all of these reporting systems are subject to bias and no direct links to the vaccine can be established. The most common published case reports were associated with CVST.<sup>43,45-48</sup>

At this moment, the pathophysiology of vaccine-induced thrombotic thrombocytopenia remains unknown. Given the clinical and biochemical similarities to heparin-induced thrombocytopenia (HIT), a similar immune-mediated response by these adenoviral vector vaccines has been



hypothesized as immune complexes with a mixture of antibody specificities similar to HIT were found in the serum of patients who developed VITT.<sup>46</sup> Platelet factor-4 (PF4) is a positively charged tetrameric protein that normally repels each other.<sup>49</sup> However, with the availability of negatively charged (polyanionic) molecules like heparin, pentosan polysulfate, or endogenous polyphosphates, PF4 can form higher-order structures that act as neoantigens. As a result, antibodies against platelet factor 4 are produced, which activate platelets and encourage clotting.<sup>50</sup> Double-stranded DNA, like heparin, is negatively charged and forms DNA/PF4 complexes, with its adjuvanticity presumably contributing to the development of autoantibodies, and eventually leading to VITT.<sup>51-53</sup>

All current vaccines, whether DNA- or RNA-based, result in spike protein production to trigger protective immunity. COVID-19 spike protein enhances host cell entry via the Angiotensin-Converting Enzyme 2 (ACE2) receptor in viral infection.<sup>54</sup> Moreover, a solid argument was made for COVID-19 spike-protein-mediated endothelial ACE2 receptor downregulation, which predisposes an individual to vasospasm and thrombotic events.<sup>55</sup> However, in clinical trials, the 2 spike-protein-targeting COVID-19 mRNA vaccines have not been associated with thrombotic immunopathology.<sup>56</sup> Another theory includes the COX-2 gene. COX-2 gene expression is known to be induced by coronavirus spike protein.<sup>57</sup> COX-2 expression is increased in newly generated platelets during normal human megakaryopoiesis.<sup>58</sup> While only around 10% of circulating platelets in healthy people express COX-2, this number is up to 60% in individuals with excessive platelet production.<sup>58</sup> COX-2 inhibition significantly reduces thromboxane A2 (TxA2) production by platelets in individuals with enhanced megakaryopoiesis compared to healthy people.<sup>58</sup> As a result, it is believed that the production of spike protein causes megakaryocytes to produce COX-2 and TxA2. TxA2 increases the synthesis of COX-2-expressing activated platelets leading to platelet activation and aggregation, and eventually resulting in thrombo-inflammation.<sup>58</sup>

## **Other Cardiovascular Complications Related to COVID-19 Vaccines**

Over the past few months, vascular thrombosis, myocarditis and pericarditis occupied the top discussions among the medical community for the major cardiovascular (CV) complications that might be related to covid vaccines. However, there are other possible post-COVID vaccination CV complications that need to be highlighted and taken into consideration.

## *Hypertension*

In June 2021, Meylan and his colleagues reported the incidence of stage III hypertension within a few minutes of the vaccination in 9 patients of a total 12,349 patients who received the covid vaccine in the same center. Eight of them were symptomatic. All patients received mRNA vaccines, 8 received Pfizer/BioNTech and 1 received Moderna vaccine. The median age was 73 years old. Blood pressure (BP) was measured using an oscillometric manometer with at least 3 sets of separate values and 5 minutes apart. No prevaccination BP values were available but 8 patients reported well-controlled BP before.<sup>59</sup> In July 2021, Kaur and his colleagues extracted the data for CV complications after the 3 common covid vaccines (Pfizer/BioNTech, Moderna, and AstraZeneca) from VigiBase, a global pharmacovigilance database maintained by World Health Organization (WHO). Hypertension has been reported in 283 (5.82% of total CV complications) patients, 93 of them have been reported as severe hypertension. The incidence of hypertension was noted to be associated with vaccine use in both genders and all different age groups<sup>1</sup>. As of September 10, 2021, a total of 5272 cases of hypertension had been reported to VAERS in the US. 72 episodes were reported as hypertensive crisis and 45 episodes were reported as hypertensive urgency (Table 1).<sup>18</sup> Until September 10, 2021, the Case Series Drug Analysis Print published by United Kingdom (UK) government for AstraZeneca vaccine, reported a total of 941 hypertensive events, 14 events were a hypertensive crisis, 4 events of hypertensive urgency, and 4 events of malignant hypertension (Table 2).<sup>44</sup> Stress is likely a contributing factor for hypertension in the setting of the public debate and white coat effect in addition to the pain associated with the injection. Another probability could be related to the comorbidities, including hypertension of the selected patients.<sup>1,59</sup> Other theories including hypertension reaction to vaccine components (polyethyleneglycol and S-protein) is unlikely as many events have been reported within minutes of the injection, leaving no time for these reactions.<sup>59</sup>

## *Acute Coronary Syndrome*

Acute coronary syndrome (ACS) and myocardial infarction (MI) in particular is one of the most dreaded cardiac complications. The initial data from clinical trials by Pfizer and Moderna in the FDA briefing documents demonstrated that the incidence of MI was 0.02% and 0.03%, respectively in the vaccine group.<sup>60,61</sup> In March 2021, 2 cases of MI had been published. Tajestra et al. reported a case of triple coronary artery thrombosis in

an 86 years old male who collapsed 30 minutes after administration of first dose of Pfizer vaccine.<sup>62</sup> Boivin et al. reported a MI case in 96 years old women 1 hour after receiving the Moderna vaccine.<sup>63</sup> Three other cases of MI have been published since that time.<sup>64,65</sup> The VigiBase database of WHO demonstrated 13 (0.27% of total CV complications) patients with angina pectoris, 32 (0.66%) patients with MI, and 16 (0.33%) patients with acute MI.<sup>1</sup> A total of 1125 cases of MI (737 were acute MI) have been reported to VAERS (Table 1).<sup>18</sup> The case series by UK for AstraZeneca vaccine report 219 (none fatal) cases of angina pectoris, 386 (51 fatal) cases of MI, and 79 (13 fatal) cases of acute MI (Table 2).<sup>44</sup> Still, it is not clear if there is any link between covid vaccines and myocardial infarction. Multiple theories have been suggested. The same mechanisms for vaccine-associated thrombosis as discussed above can explain the current cases of MI. Kounis syndrome, as an allergic or anaphylactic reaction to the vaccine, could be another possibility. Kounis syndrome can cause MI through different mechanisms like allergic vasospasm and stent occlusion with a thrombus infiltrated by eosinophils and/or mast cells.<sup>66,67</sup> In addition, Boivin and his colleagues suggested that the stress of getting the vaccine in elder people with other associated comorbidities can lead to demand-supply mismatch ischemia.<sup>63</sup>

### *Stress Cardiomyopathy “Takotsubo Cardiomyopathy”*

In May 2021, Jani and his colleagues reported a case of stress cardiomyopathy in 65 years old women within 2 days of the first dose of Moderna vaccine. She presented with chest pressure and bradycardia. She was found to have inferolateral ischemia on EKG, new-onset hypokinesia of mid and distal segments of the left ventricle on echocardiography, and only mild coronary artery disease on coronary angiography. No unusual physical or emotional stress was reported.<sup>68</sup> As of June 10, 2021, Vidula and his colleagues have reported a case of stress cardiomyopathy in a 60 years old woman. She presented with severe chest pain 4 days after the second dose of Pfizer vaccine. She was found to have new inferolateral T wave inversions on EKG and apical akinesis on echocardiography (not shown in her previous echo 5 months prior) with no obstructive disease found on coronary angiography.<sup>6</sup> A total of 39 cases of stress cardiomyopathy have been reported to VAERS (Table 1).<sup>18</sup> The case series by UK for AstraZeneca reported 5 cases of stress cardiomyopathy with none of them being fatal (Table 2).<sup>44,69</sup> Stress cardiomyopathies have been reported previously with other vaccines like Influenza, tetanus, diphtheria, polio, and hepatitis B vaccines.<sup>70</sup>

## Arrhythmias

Multiple reports have described the incidence of different arrhythmias after covid vaccines use. Per the VigiBase database of WHO, Kaur and his colleagues reported 717 events of palpitations, 185 of them have been reported as serious events.<sup>1</sup> A total of 11,252 events of palpitation have been reported to VAERS (Table 1).<sup>18</sup> The case series by UK for AstraZeneca vaccine reported 5157 events of palpitation, only 1 event was fatal (Table 2).<sup>44</sup> The most commonly reported arrhythmias were tachycardia, sinus tachycardia, atrial fibrillation (AF) and supraventricular tachycardia.<sup>1,18,44</sup> Lastly, Li and his colleagues reported the incidence of AF after Vero Cell vaccine in a 31 years old gentleman with Marfan syndrome and status post Bentall operation and mitral valve replacement. Prevacination EKG was clear of arrhythmia but 8 hours after the vaccination he developed palpitation with EKG showing AF with a rapid ventricular response.<sup>71</sup> It is unclear if the arrhythmic events reported are purely related to the covid vaccines or related to underlying cardiac comorbidities with coincidental timing after vaccine administration. The prevalence of baseline rhythm abnormalities among general populations is 2.35% and the prevalence of AF among people over 40 and 65 years old is 2.3% and 5.9%, respectively.<sup>72,73</sup> The prevalence is much lower after COVID-19 vaccine. According to VAERS, the prevalence of palpitations and atrial fibrillation are 0.006% and 0.0009%, respectively.<sup>18</sup>

## Cardiac Arrest and Death

The initial data from the clinical trial by Pfizer for its vaccine demonstrated 1 event of cardiac arrest and 2 deaths. Reports indicated that death occurred at the same rate as in the general population.<sup>61</sup> As of April 2021, Edler and his colleagues in Germany reported 3 cases of death after covid vaccine administration within 15 days. All of them had a history of severe cardiovascular diseases and other comorbidities. Two patients (1 tested negative for COVID) were found on the postmortem forensic exam to have a pulmonary embolism (PE) and recurrent MI as the cause of death. The third patient died from covid infection within 10 days after vaccine administration. The authors did not report what type of vaccine was administered.<sup>74</sup> Kaur et al. reported 35 (0.72% of total CV complications) events of cardiac arrest.<sup>1</sup> The case series by UK for AstraZeneca vaccine reported 301 cases of death and 167 (35 of them were fatal) cases of cardiac arrest (Table 2).<sup>44</sup> As of September 10, 2021, the CDC reported 6181 cases of deaths and 830 cases of cardiac arrest among people who received the vaccine according to VAERS (Table 1).<sup>18</sup> Some recent

reports pointed towards thrombosis with VITT as the cause of death.<sup>75</sup> No more case reports about postvaccination deaths and cardiac arrests could be found in the literature. No evidence of direct correlation with the vaccine has been found.

## Conclusion

It is crucial to understand a few points. First, the purpose of this review article is to increase awareness among health care workers about the possible cardiovascular events postvaccination. Second, the vaccine was initially given to the elderly and high-risk populations, so it is expected that this age group will have cardiovascular events. Such vulnerable populations are more amenable to develop adverse effects from medication in general. Though our review did not show this correlation for all CV adverse effects, some adverse effects such as MI and arrhythmias were more commonly seen in these already vulnerable population. While other cardiovascular events such as myocarditis or vaccine-induced thrombotic thrombocytopenia were more common in younger populations. Third, compared with the total number of vaccine doses given, the incidence of all reported cardiovascular adverse events remains very rare. Finally, a direct causal relationship, if any, between vaccination and the adverse events is yet to be fully elucidated. All presented data are from case reports and the reporting systems. Thus, based on our review, we conclude that the benefits of vaccination far outweigh the risk at this time.

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