DHA-IHD
20 OCT 2021

INFORMATION PAPER
ON
OPTIONS FOR COVID-19 VACCINATION FOLLOWING MYOPERICARDITIS

ISSUE:

Myocarditis is a heterogeneous disease with diverse clinical patterns (including, but not limited to, chest pain, shortness of breath, and/or heart palpitations), etiologies, and therapeutic responses, reflecting inflammatory injury to myocardial tissue in the absence of ischemia. While viral infections, including SARS-CoV-2, are the most common cause of the myocardial inflammation, myocarditis has also been associated with certain drugs and vaccines, most notably the smallpox vaccine. Myocarditis associated with COVID-19 vaccines, principally the mRNA vaccines, has now been identified, albeit a rare event.

BACKGROUND:

Introduction

Safety surveillance reports received by the DHA, FDA and CDC identified a risk for myocarditis and pericarditis following administration of COVID-19 vaccines, particularly mRNA vaccines. Reports of confirmed myocarditis/pericarditis in VAERS have been higher among males under 40 years of age than among females and older males. Males 12-29 years of age seem at highest risk, particularly following the second dose. Onset of symptoms generally occurs within 7 days following vaccination. Although a few cases of vaccine-associated myocarditis/pericarditis have required intensive care support, the majority of hospitalizations were for diagnostic testing as the nature of vaccine-associated myocarditis was being determined. In the majority of patients, symptoms (chest pain, dyspnea, and/or palpitations) were considered to be mild to moderate. Importantly, individuals had resolution of symptoms within days to weeks with conservative management. The mechanism of action by which the vaccine could cause myocarditis/ pericarditis has not been established. Follow-up is ongoing to identify and understand any potential long-term consequences. [1]

It is also important to note that most pre-existing cardiac conditions are not regarded as contraindications to vaccination. The American Heart Association and CDC recommend people with cardiovascular risk factors, heart disease including stable heart failure, arrhythmias, most congenital heart disease, heart attack and stroke survivors and people with implantable cardiac devices should get vaccinated as soon as possible because they are at much greater risk from the virus than they are from the vaccine.

Myocarditis/Pericarditis Case Definitions

	Probable	Confirmed
Acute Myocarditis	Presence of ≥1 new or worsening of the following symptoms: • chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations AND ≥1 new finding of • Elevated troponin level • Abnormal EKG findings consistent with myocarditis • Abnormal cardiac function or wall motion abnormalities on echocardiogram • cMRI findings consistent with myocarditis AND • No other identifiable cause of the symptoms and Findings	Presence of ≥1 new or worsening of the following symptoms: • chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain w/ breathing • palpitations AND ≥1 new finding of • Histopathologic confirmation of myocarditis • cMRI findings consistent with myocarditis in the presence of troponin level above upper limit of normal AND • No other identifiable cause of the symptoms and findings
Acute Pericarditis	Presence of ≥2 new or worsening of the following clinical features: • acute positional or pleuritic chest pain • pericardial rub on exam • new ST-elevation or PR-depression on EKG (not c/w early repolarization) • new or worsening pericardial effusion on echocardiogram or MRI	

Refer to DHA-IHD Vaccine-Associated Myopericarditis Diagnostic & Treatment Algorithm for guidance in diagnosis and management of suspected post-vaccination Myopericarditis.

Estimated (order of magnitude) incidence of myocarditis
Myocarditis after SARS-CoV-2 infection occurs in approximately 1 in 100 young athletes [2]
Myocarditis after smallpox vaccine occurs clinically in approximately 1 in 1,000 vaccinees [3]
Myocarditis after the 2nd dose of an mRNA COVID-19 vaccine occurs clinically in approximately 1 in 10,000 young males [4]
Comparing risk of myocarditis from COVID-19 disease vs vaccination; there is approximately a 10-fold higher risk of myocarditis from infection for individuals of all ages and gender [5] vice an approximately 100-fold higher risk found in the smaller cohort of young adult males.

CDC guidance [6]
(1) History of myocarditis or pericarditis prior to COVID-19 vaccination
(a) People who have a history of myocarditis or pericarditis unrelated to mRNA COVID-19 vaccination may receive any currently FDA-approved or FDA-authorized COVID-19 vaccine after the episode of myocarditis or pericarditis has completely resolved. This includes resolution of symptoms attributed to myocarditis or pericarditis, as well as no evidence of ongoing heart inflammation or sequelae [as assessed clinically and through special testing to assess cardiac recovery].

(2) Myocarditis or pericarditis after receipt of the first dose of an mRNA COVID-19 vaccine series, but before administration of the second dose.

(a) It is unclear if people who developed myocarditis or pericarditis after a first dose of an mRNA COVID-19 vaccine may be at increased risk of further adverse cardiac effects following a second dose of the vaccine. Until additional safety data are available, [CDC recommends] that people who develop myocarditis or pericarditis after a first dose of an mRNA COVID-19 vaccine defer receiving the second dose.

(b) Administration of the second dose of an mRNA COVID-19 vaccine series can be considered in certain circumstances. Considerations for vaccination may include:

- Personal risk of severe acute COVID-19 (e.g., age, underlying conditions)
- Level of COVID-19 community transmission and personal risk of infection

(c) People with a history of myocarditis or pericarditis who choose to receive the second dose of an mRNA COVID-19 vaccine should wait at least until their episode of myocarditis or pericarditis has completely resolved. [See DHA-IHD Vaccine-Associated Myopericarditis Diagnostic & Treatment Algorithm] This includes resolution of symptoms attributed to myocarditis or pericarditis, as well as no evidence of ongoing heart inflammation or sequelae [as assessed clinically and through special testing to assess cardiac recovery]. Decisions about proceeding with the second dose should include a conversation between the patient and clinical team.

(3) CDC does not address the more common situation of the development of myocarditis following the second dose of mRNA COVID-19 vaccine and subsequent [booster] doses. However, at this time we assume guidance would be the same as above. Potentially having bearing on this decision, preliminary data from an ongoing study suggests myocarditis following a 3rd dose of an mRNA COVID-19 vaccine (in an older population without prior myocarditis) is extremely rare (1:2M 3rd doses) [7]

(4) CDC does not address the option of using Janssen vaccine in the case of an mRNA-associated myocarditis. The CDC does, however, take the position that, in limited, exceptional situations where a patient received the first dose of an mRNA COVID-19 vaccine but is unable to complete the series with either the same or different mRNA COVID-19 vaccine, a single dose of Janssen COVID-19 vaccine may be given, and the patient be considered to be fully vaccinated against COVID-19. However, this does not address the likelihood, or not, of a myocarditis recurrence.

DISCUSSION:

A. Risk Assessment regarding subsequent vaccination in an individual who develops Myopericarditis following receipt of a COVID-19 vaccine. What is the risk associated with:

(1) *No further mRNA COVID-19 vaccine* – results in under-immunization. One-dose efficacy for mRNA vaccines is at least 51% against SARS-CoV-2 infection and 54% against COVID-19 illness. [8] Duration of whatever immunity might be present is at least 16 weeks post-vaccination. [9] Risk of serious disease following a single mRNA COVID-19 vaccination is dependent upon individual's comorbidities and other risk factors, exposure risk, and exposure-mitigating behavior.

(2) *Provision of subsequent mRNA vaccine* – provides adequate level of immunity. Two-dose efficacy for mRNA vaccines is >90% effective against hospitalization. [10] Duration is >24 weeks of protection against severe COVID-19 illness requiring hospitalization. [11] Risk of break-through disease is approximately 10%.
Risk of recurrence of Myopericarditis with subsequent mRNA vaccination. There is at least one report of recurrence of myocarditis within 48 hrs of receipt of dose #2 in 17 y/o male who developed myocarditis with dose #1 four months earlier. [12] Among 112 post-SPV myocarditis patients in the IHD Natural History Registry for whom complete COVID-19 vaccination records were available*, 107 were fully vaccinated with an mRNA vaccine (either Pfizer or Moderna), and 5 with Janssen vaccine. Of this 112 fully-vaccinated group; 1 developed myocarditis (Moderna) and 2 met criteria for pericarditis (Pfizer, Moderna), but were indeterminate for myocarditis due to delays in evaluations. [*unpublished data not peer-reviewed]

(3) *Provision of a subsequent non-mRNA vaccine* (e.g., Janssen vaccine) – provides adequate immunity. A single dose of Janssen vaccine was found to have an efficacy of 67% against symptomatic moderate disease, 85% efficacy against severe disease and 93% efficacy against hospitalization. [13] While one dose of the Janssen vaccine would satisfy 'series completion', very little data yet exists assessing the safety or efficacy of the Janssen vaccine following one dose of mRNA vaccine. A preliminary study comparing resulting antibody levels between another viral-vectored vaccine similar to the Janssen vaccine (two-dose AstraZeneca) and an mRNA vaccine (Pfizer) showed those who received an mRNA vaccine followed by the viral-vectored vaccine did not develop as high an antibody level as seen with two doses of an mRNA vaccine (Geometric Mean Concentration (GMC) 7,133 ELU/ml vs 14,080 ELU/ml). However, the GMC of the heterologous combination was higher than that of the two-dose AstraZeneca vaccine which does have proven efficacy against COVID-19 disease and hospitalization. [14]
Risk of myocarditis with Janssen vaccine appears very low. A recent literature review of 23 articles (11 case series and 12 case reports with a total of 81 patients) [15] identified only one individual with myocarditis following administration of the Janssen vaccine. [16] Among the 56 patients the IHD is following, there are 4 pericarditis cases and 1 myocarditis case associated with Janssen vaccine.
However, the impact of receiving the Janssen vaccine following developing myocarditis with an mRNA COVID-19 vaccine has not been studied.

RECOMMENDATIONS:

Counsel individual on risk and benefits of above options (shared decision making). Before an option to vaccinate is considered, individual should be cleared for return to normal activity/full duty IAW DHA-IHD Vaccine Associated Myopericarditis Diagnostic & Treatment Algorithm (minimum post-vaccination interval of 90 days)

(1) An individual with a history of myocarditis not associated with receipt of an mRNA COVID-19 vaccine may receive any currently FDA-approved or FDA-authorized COVID-19 vaccine after the episode of myocarditis or pericarditis has completely resolved. Assure the patient has been cleared to return to active duty or resume normal

activities and all clinical symptoms are resolved. Assure cardiac labs/imaging studies are normal. Assure the individual has returned to baseline exercise tolerance. Provide the vaccine. No special studies, pre-treatment, or post treatment studies required.

(2) For people who develop myocarditis or pericarditis after a dose of an mRNA COVID-19 vaccine, the recommendation is to defer receiving a subsequent dose of any COVID-19 vaccine unless there exists certain circumstances placing them at high risk if not fully vaccinated. As presently there is no definitive point in time by which we expect to have sufficient data to address this issue, if patient elects no further vaccination, the IHD recommends that a permanent medical exemption (MP) be entered into the EHR until accepted best practices in the medical literature can address the safety of subsequent mRNA doses, or provides other options. Counsel patient on the necessity of strict adherence to adjunctive methods to reduce risk of SAR-CoV-2 infection; e.g., masking, social distancing, frequent handwashing.

(3) For those who are at increased exposure or disease outcome risk, and who, after appropriate counseling, including acknowledging the current lack of data regarding the risk, or not, of myocarditis recurrence with subsequent vaccination, elect to receive either a subsequent mRNA vaccine or a single dose of the Janssen vaccine; providers must assure the patient has been cleared to return to active duty or resume normal activities and all clinical symptoms are resolved IAW the DHA-IHD **Vaccine Associated Myopericarditis Diagnostic & Treatment Algorithm**. Assure all cardiac labs/imaging studies are normal. Assure the individual has returned to baseline exercise tolerance. No special studies, pre-treatment, or post treatment studies are required. Closely follow up for 30 days.

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