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Myocarditis and pericarditis after mRNA COVID-19 vaccination in children: Interim guidance

Version 3.3.
August 6th 2021

Summary statements for clinicians

1. **How should cases be identified?**
   - Any patient who presents with acute chest pain, palpitations, dyspnea, syncope or diaphoresis within 42 days after receiving a COVID-19 mRNA vaccine should be evaluated in-person for the possibility of myocarditis or pericarditis.
   - Patients with pericarditis usually have an abnormal ECG, and normal to mildly elevated troponins. Patients with myopericarditis may have an abnormal ECG result and have significantly elevated troponins with normal left ventricular function on the echocardiogram. Patients with myocarditis typically have an abnormal ECG, elevated troponins, and decreased left ventricular function on the echocardiogram.

2. **What are the recommended investigations?**
   - An ECG and troponin level should be performed in any patient with a suspicion of myocarditis or pericarditis following COVID-19 vaccination. For patients who present with fever, a CBC with differential, CRP, blood culture, sodium and albumin levels should also be performed.
   - Patients with a normal ECG and normal troponin levels do not need any further investigation.
   - Patients with an abnormal ECG and/or elevated troponin levels who are otherwise stable should have an echocardiogram performed within 48h. Patients who are hemodynamically unstable should have an echocardiogram performed urgently.

3. **What is the management?**
   - Most cases are self-limited and respond to nonsteroidal anti-inflammatory agents (NSAIDs). In some cases, colchicine may be considered on a case-by-case basis in discussion with cardiology.
   - Corticosteroid use should be avoided.

4. **Which patients should be seen by a cardiologist? Which patients need to be transferred to SickKids?**
   - Patients with a normal ECG and normal troponin levels do not need to be referred to a cardiologist.
   - Patients with an abnormal ECG and/or elevated troponin levels should be referred to a cardiologist for an echocardiogram. This can be performed as an outpatient in a community setting within 48h if the patient is well clinically.
   - In settings in which an echocardiogram or a cardiologist are not readily available, patients may be referred to the cardiology clinic at SickKids (or their local paediatric centre).
   - Any child with cardiac dysfunction or more than a small pericardial effusion seen by echocardiography should be discussed with cardiology at SickKids (or their local paediatric centre) to determine timing and location of cardiology assessment.
   - Any child with hemodynamic instability should be discussed with SickKids (or their local paediatric centre) via *Criticall* as per standard practice.

5. **Which patients should be reported to Public Health as an Adverse Events Following Immunization?**
   - Any patient with confirmed myocarditis or pericarditis following COVID-19 vaccination should be reported to Public Health as an Adverse Event Following Immunization (AEFI).
   - Patients who present with symptoms of myocarditis or pericarditis but with normal ECG and normal troponins may also be reported on a case-by-case basis, as deemed appropriate by the treating physician. It should be noted that all cases reported as an AEFI to Public Health will undergo thorough review for causality assessment between vaccination and presenting symptoms.

6. **What should be done with the second dose of the COVID-19 vaccine?**
   - For now, the National Advisory Committee on Immunization (NACI) has recommended for the second dose of mRNA COVID-19 vaccination to be deferred in children who experience myocarditis or pericarditis following the first dose until more information is available.
   - Patients with confirmed myocarditis or pericarditis can also be referred to a Special Immunization Clinic (SickKids, McMaster Children's Hospital or Children's Hospital of Eastern Ontario) for causality assessment and further guidance on future doses of COVID-19 vaccines.

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1. Introduction

Since April 2021, there are increasing reports of cases of myocarditis and pericarditis after mRNA COVID-19 vaccination (Pfizer-BioNTech BNT162b2 vaccine and Moderna mRNA-1233 vaccine).[1-5] In Canada, there have been a small number of these reports.[6-8] The Public Health Agency of Canada (PHAC), Health Canada and Public Health Ontario (PHO) are closely monitoring these rare events, including those among youth. To date, PHO has received reports of a number of cases of myocarditis/pericarditis in the 12 to 17 age group in Ontario through the provincial surveillance of Adverse Event Following Immunization (AEFI).[6] The Centers for Disease Control (CDC) in the United States have also reported an increased risk of myocarditis and pericarditis in the 7 days after receipt of dose 1 or dose 2 of an mRNA COVID-19 vaccine, particularly among younger males after dose 2.[9] A summary table of published case series on myocarditis and pericarditis following COVID-19 mRNA vaccination can be found in the supplementary information (Table 1).

Preventing the spread of COVID-19 remains extremely important, and in Canada, the National Advisory Committee on Immunization (NACI) **continues to recommend COVID-19 vaccines continue for all eligible individuals, including youth**.[10] Other countries using mRNA vaccines in young adults and adolescents are also continuing to recommend their use but are following the emerging evidence on this topic very closely as further information is obtained.[9] The benefits of the mRNA vaccines continue to outweigh their risks in the authorized populations, as there are clear benefits of mRNA vaccines in reducing deaths and hospitalizations due to COVID-19 infections.

This document aims to provide interim guidance based on consensus opinion for clinicians who will be assessing pediatric patients who develop myocarditis or pericarditis after mRNA COVID-19 vaccination and should not replace best clinical judgment. This document will be revised as further information on this condition is gained. The management and clinical decision algorithm can be found at the end of this document.

2. Case definitions

International and national reports of myocarditis/pericarditis following vaccination with COVID-19 mRNA vaccines have emerged.[1,6,8] These reports indicate that:

- Cases have been seen after the first dose of a COVID-19 mRNA vaccine, but are more commonly reported after the second dose
- Symptom onset was typically within several days after vaccination, with most cases being reported within **7 days** after vaccination
- Cases were mainly adolescents and young adults
- Cases were more often males compared to females
- Cases experienced mild illness, responded well to conservative treatment and rest, and their symptoms improved quickly.

Myocarditis and pericarditis involve inflammation of the myocardium or the pericardium, respectively, in response to an infection or some other trigger. Symptoms can include shortness of breath, chest pain, or the feeling of a rapid or abnormal heart rhythm. Myocarditis and pericarditis may overlap in clinical practice. Cases of pericarditis with an associated elevation of troponins, in the absence of reduced left ventricular function may be designated as **myopericarditis**. The clinical definition and classification for pericarditis, myopericarditis and myocarditis are detailed and represented in Table 1.

Until further data is gathered and a definition for an Adverse Event of Special Interest for myocarditis/pericarditis following COVID-19 vaccination has been established, patients who develop pericarditis or myocarditis up to **42 days (6 weeks)** after vaccination should follow this guidance and should

be reported to public health.[11,12] It should be noted that the peak incidence occurs 1-3 days after vaccination and up to 7 days; cases beyond this are expected to be rare and other diagnoses should be considered.

Pericarditis:

The diagnosis of acute pericarditis can be made in the presence of at least two of the following four criteria, as described in the European Society of Cardiology and American College of Cardiology Guidelines for Pericardial Disease[8]:

1. Pericarditic chest pain (sudden in onset, retrosternal, and pleuritic exacerbated by inspiration)
2. Pericardial rub found at auscultation
3. ECG changes including widespread ST-segment elevation or PR depression (See below)
4. New or worsening pericardial effusion at echocardiogram

Some of the supportive findings also include an elevation of inflammatory markers (CRP, ESR, white blood cell count). However, it should be noted that many of the reported cases of pericarditis after mRNA vaccination have had normal or mildly elevated inflammatory markers, and therefore a normal CRP, ESR and/or CBC does not rule out this diagnosis.[2] Patients who present with pericarditis usually have **normal or mildly elevated troponins and normal left ventricular (LV) function**. For reference, the Brighton collaboration case definitions for definitive, probable and possible cases of pericarditis, which is used as a framework for case definition by Public Health Ontario, are also detailed in Table 2 in the supplementary information.

ECG changes that may be seen in pericarditis:

- Widespread concave ST elevation and PR depression throughout most of the limb leads (I, II, III, aVL, aVF) and precordial leads (V2-6)
- Reciprocal ST depression and PR elevation in lead aVR (± V1)
- Sinus tachycardia
- Low voltages

Myocarditis:

Myocarditis can present as different clinical syndromes that range from mild chest pain with transient ECG changes to heart failure and cardiogenic shock.[13] Patients with myocarditis have **ECG changes that are consistent with myocarditis** (see below) and/or **elevation of their troponins**. Patients are often found to have a **decreased left ventricular function** at their echocardiogram.[14] For reference, the Brighton collaboration case definitions for definitive, probable and possible cases of myocarditis, which is used as a framework for case definition by Public Health Ontario, are also detailed in Table 3 in the supplementary information.

ECG changes that may be seen in myocarditis:

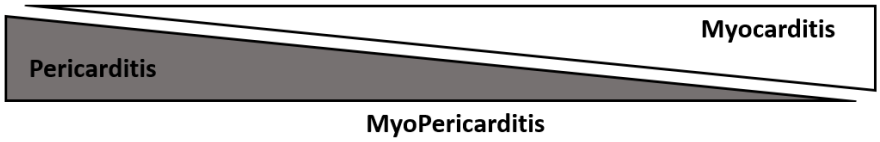
- Paroxysmal or sustained atrial or ventricular arrhythmias (premature atrial or ventricular beats, and/or supraventricular or ventricular tachycardia, interventricular conduction delay, abnormal Q waves, low voltages)
- AV nodal conduction delays or intraventricular conduction defects (atrioventricular block (grade I-III), new bundle branch block)
- ST segment and T waves changes
- Prolonged QRS
- QT prolongation
- Diffuse T wave inversion

Myopericarditis:

Patients who present with **clinical and ECG features of pericarditis or myocarditis** as detailed above, and who have **significantly elevated troponins** are considered to have myopericarditis.[15] However, patients with myopericarditis may have a pericardial effusion at their echocardiogram as seen in pericarditis, but **do not have decreased left ventricular function**. The management of myopericarditis is similar to that of pericarditis, as detailed in section 4 of this document.

Table 1: Usual characteristics of pericarditis, myopericarditis and myocarditis

	Pericarditis	MyoPericarditis	Myocarditis
ECG result	Abnormal (findings in keeping with pericarditis)	May be abnormal (findings in keeping with pericarditis or myocarditis)	Abnormal (findings in keeping with myocarditis)
Troponins	Normal or mildly elevated	Significantly elevated	Significantly elevated
Echocardiogram	Normal LV function May have pericardial effusion	Normal LV function May have pericardial effusion	Decreased LV function



* Adapted from *Imazio et al* (J Cardiovasc Med, 2014)[15]

Other features and association with MIS-C (Multisystem Inflammatory Syndrome in Children):

Based on the reports received, patients who developed myocarditis/pericarditis after COVID-19 mRNA vaccination do not seem did not present the features of MIS-C. However, given the paucity of data available currently, it is important to ensure that these patients do not present any signs and symptoms of MIS-C. These symptoms include persistent fever, abdominal pain, vomiting, diarrhea, neurological symptoms (including altered mental status, lethargy, encephalopathy, focal neurological deficits and meningismus), skin rash, mucocutaneous lesions and in some severe cases, hypotension and shock.[16]

3. Recommended investigations

All patients who present with symptoms concerning for pericarditis or myocarditis in the following days after COVID-19 mRNA vaccination should be assessed in-person by a physician. An **ECG** and serum **troponin I** should be performed in all patients with a clinical suspicion of post-vaccination myocarditis or pericarditis, based on the symptoms and criteria detailed above. A nasopharyngeal swab for SARS-CoV-2 PCR should be considered in these patients, depending on the presenting symptoms. A blood culture**,** a complete blood count (CBC) and differential, CRP, sodium, albumin and peripheral IV insertion should be performed in patients who present with fever.

Patients with normal ECG and normal or mildly elevated troponins do not require any further investigations, activity modifications, follow up or referral to cardiology. These patients may be considered to have chest pain following COVID-19 mRNA vaccination and may require investigations for consideration of another diagnosis, as deemed appropriate.

Patients who have an **abnormal ECG (as detailed above) and/or significantly elevated troponins (≥100 ng/L)** should be referred to a cardiologist **for an echocardiogram to be performed**. In patients who are otherwise

well clinically, the echocardiogram can be performed in an outpatient setting **within 48h of presentation**, either in a community setting or at the cardiology clinic at SickKids. In settings in which an echocardiogram or a cardiologist are not readily available, patients may be referred to the cardiology clinic at SickKids through the usual process for patient referral. **Routine serial troponin monitoring is not recommended except in rare instances in consultation with Cardiology**.

Patients with an abnormal ECG and/or elevated troponins should also be discussed with infectious diseases regarding any further investigations that may be required on a case-by-case basis and to organize the outpatient follow-up at the Special Immunization Clinic. SARS-CoV-2 serology testing (anti-SARS-CoV-2 IgG and anti-nucleocapsid antibodies) should also be performed for patients with a confirmed diagnosis of pericarditis and/or myocarditis, in discussion with infectious diseases and the microbiologist on-call. The COVID-19 biobank study team may be notified about these patients as appropriate for possible enrolment.

Patients with a normal echocardiogram, regardless of the ECG findings and troponin levels, do not require any additional investigations **UNLESS there is fever and/or features of MIS-C**. If so, please follow recommendations for the MIS-C pathway for expanded investigations (see below and link). **There is no role for serial troponin monitoring in the setting of a normal echocardiogram.**

Patients with an **abnormal echocardiogram should be referred to SickKids for evaluation by cardiology.** If admission is warranted for cardiac reasons (see below), patients should be admitted under cardiology, and infectious diseases and rheumatology should be consulted. Further investigations for causes of myocarditis for patients with borderline or mildly reduced heart function may be considered, as clinically indicated and in consultation with cardiology, rheumatology and infectious diseases (See box 1 in the supplementary information).

Patients with an abnormal ECG and/or elevated troponins **and with any features of MIS-C** as detailed above should be discussed with rheumatology, and management should be in accordance with the COVID-associated hyperinflammation / Kawasaki Disease pathway (SickKids SharePoint). In addition to the bloodwork detailed above, expanded bloodwork for COVID-associated hyperinflammation also includes the following:

- Potassium, creatinine, ALT, LDH
- NT-pro-BNP
- Fibrinogen, D-dimers, PTT, INR
- Ferritin, triglycerides, ESR

4. Management

Pericarditis and myopericarditis:

In general, most cases of acute pericarditis are self-limited and respond to nonsteroidal anti-inflammatory agents (NSAIDs). In cases of mild pericarditis, ibuprofen can be started using the dosing below, and patients can be followed in an ambulatory setting as detailed in the following section.

Ibuprofen: 10 mg/kg/dose q8h x 1 week (max 600mg), then 7.5 mg/kg/dose q8h x 1 week (max 400mg), then 5 mg/kg/dose q8h x 1 week (max 200mg).

In some cases, colchicine may be considered on a case-by-case basis and in discussion with cardiology. Colchicine has been observed to be effective in relieving pain and preventing recurrent pericarditis.[17,18] However, no data is currently available on its use in the context of pericarditis occurring after COVID-19 mRNA vaccination.

Admission for observation and further investigations in consultation with cardiology, infectious diseases and rheumatology should be considered in cases who present high and persistent fevers, evidence of a large

pericardial effusion at echocardiogram, clinical evidence of cardiac tamponade, and in the absence of response to NSAIDs and/or colchicine.

Corticosteroid use should be avoided as a first-line option in children given their association with increased risk of recurrences of pericarditis. In discussion with cardiology, steroids may be considered in select cases as a second-line option in the absence of response to NSAIDs or colchicine.[19]

Myocarditis:

The treatment of myocarditis should be decided on a case-by-case as it is guided by the severity of the presentation. For mild cases without decreased heart function or features of heart failure, NSAIDs may provide symptomatic relief and patients may be followed in an ambulatory setting. In general, most cases of myocarditis following COVID-19 mRNA vaccination that have been reported have been mild and have been shown to be responsive to NSAIDs.

More severe cases with decreased heart function or displaying features of heart failure, arrhythmia or other complications of myocarditis may require hospitalization for observation, investigations and further treatments. These patients may require supportive therapy that should be determined by cardiology, including pain control, hemodynamic and/or respiratory support, heart failure management, arrhythmia management and anticoagulation.

Immunomodulatory treatment may be considered in certain cases as per institutional practice and will be recommended by cardiology as clinically indicated. Further investigations in cases of severe myocarditis requiring hospitalization should also be discussed in consultation with cardiology, rheumatology and infectious diseases (see box 1 in supplementary information).

5. Follow-up

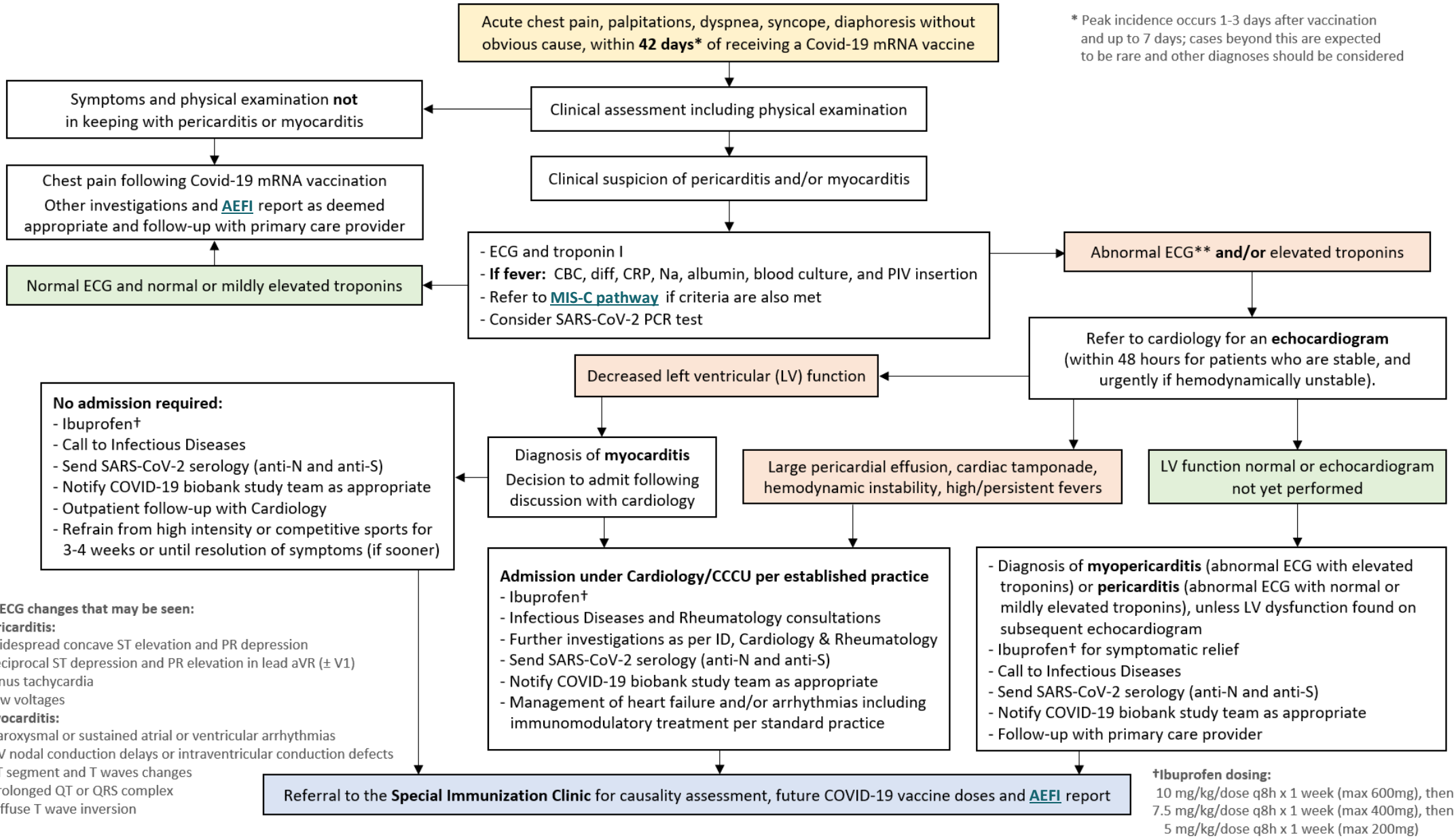
All suspected cases should be followed by their primary care physicians (PCP). Patients with a diagnosis of pericarditis should be followed by their PCP; some may warrant cardiology follow-up, but this will be determined by cardiology on a case-by-case basis, depending on the result from the echocardiogram. Patients with a confirmed diagnosis of myocarditis should also be followed by a cardiologist at an interval and frequency that will be determined by cardiology based on clinical severity, echocardiogram result and course.

Patients with a confirmed diagnosis of pericarditis or myopericarditis should refrain from high intensity or competitive sports for 3-4 weeks or until resolution of symptoms (if sooner). Patients with a confirmed diagnosis of myocarditis also require a modification in exercise, which will be recommended by cardiology on a case-by-case basis, including duration.

Every patient with a confirmed diagnosis of pericarditis, myopericarditis or myocarditis following COVID-19 mRNA vaccination should also be referred to the **Special Immunization Clinic** (SIC) to be assessed by an infectious diseases specialist. In Ontario, there are three pediatric SIC clinics, located at SickKids, McMaster Children's Hospital and Children's Hospital of Eastern Ontario (CHEO). The SIC physician will look to find the causality of the AEFI and the risk of recurrence upon revaccination for any vaccination, including for a second dose of an mRNA COVID-19 vaccine, if applicable. Currently, NACI is recommending that the second dose of the mRNA COVID-19 vaccine should be deferred in individuals who experience myocarditis or pericarditis following the first dose of an mRNA COVID-19 vaccine until more information is available.[10] Factors that could influence the decision to revaccinate include evidence of prior infection with SARS-CoV-2 (history of COVID-19 and/or positive anti-nucleocapsid antibodies), the severity of the myocarditis/pericarditis, an individualized benefit-risk analysis and a discussion with the patient and their family.[20,21]

Upon referral, the SIC physician will also **submit cases of myocarditis and pericarditis** following COVID-19 vaccines to the public health unit using the Ontario AEFI reporting form. Public Health Ontario (PHO) is monitoring this issue as part of enhanced COVID-19 vaccine safety surveillance and produces a weekly summary of all COVID-19 AEFIs in Ontario, including myocarditis/pericarditis. Patients with confirmed myocarditis or pericarditis who are not referred to the SIC should reported to their local public health unit using the AEFI reporting form. Patients who present with symptoms of myocarditis or pericarditis but with normal ECG and normal troponins may also be reported on a case-by-case basis, as deemed appropriate by the treating physician. All cases reported as an AEFI to Public Health will undergo thorough review for causality assessment between vaccination and presenting symptoms.

Algorithm for the management of patients with myocarditis, pericarditis or myopericarditis after mRNA COVID-19 Vaccination



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Supplementary information

Supplementary table 1. Summary of published case series on myocarditis / pericarditis following COVID-19 mRNA vaccination

Study	n	% Pfizer (BNT162b2)	% males	% 2nd dose	Age range (years old)	Symptom onset	Prior COVID-19	Investigations	Treatment	Symptoms resolved
Marshall et al (Pediatrics)[2]	7	100%	100%	100%	14-19	0 – 4 days	None with history of prior infection 15% anti-N positive	Abnormal troponin (100%), ECG (100%), MRI (100%), ECHO (28.6%). No positive COVID-19 PCR	All admitted NSAIDS (42.9%), IVIg + steroids (57.1%).	100%
Snapiri et al (PIDJ)[22]	7	100%	100%	85%	16-18	1 – 3 days	0%	Abnormal troponin (100%), ECG (85.7%), ECHO (42.9%). No positive COVID-19 PCR	All admitted NSAIDS (71.4%), aspirin (14.3%), no treatment (14.3%).	100%
Rosner et al (Circulation)[23]	7	71%	100%	71%	19-30	2 – 7 days	0%	Abnormal troponins (100%), ECG (71.4%), ECHO (57.1%), MRI (100%). No positive COVID-19 PCR	NSAIDS (42.9%), Colchicine (42.9%), steroids (14.3%)	100%
Larson et al (Circulation)[24]	8	62.5%	100%	88%	21-56	1 – 4 days	None with history of prior infection	Abnormal troponins, ECG (75%), ECHO (100%), MRI. No positive COVID-19 PCR	NSAIDS (3/8), Colchicine (25%), steroids (12.5%).	100%
Abu et al (Vaccine)[25]	6	100%	100%	83%	16-45	1 – 16 days	0%	Abnormal troponin (100%), ECG (100%), MRI (100%), ECHO (28.6%). No positive COVID-19 PCR	All admitted NSAIDS and colchicine (100%)	100%
Kim et al (JAMA cardiology)[26]	4	50%	75%	85%	23-70	1 – 5 days	None with history of prior infection	Abnormal troponin (100%), ECG (100%), MRI (100%). No positive COVID-19 PCR	All admitted NSAIDS (50%), Colchicine (75%), steroids (25%)	100%
Montgomery et al (JAMA cardiology)[27]	23	30%	100%	88%	20-51	1 – 4 days	None with history of prior infection	Abnormal troponins (100%), ECG (82.6%), ECHO (17.4%), MRI (100%). No positive COVID-19 PCR	N/A	70%

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Supplementary table 2: Pericarditis Brighton Collaboration case definition

Pericarditis Level of Certainty - 1 (Definitive Case)
Histopathologic examination of pericardial tissue (autopsy or pericardial biopsy) showed pericardial inflammation
OR
Abnormal testing need at least 2 of 3 of the following:
Evidence of abnormal fluid collection or pericardial inflammation by imaging (Echo, MR, cMR, CT)
OR
Electrocardiogram (EKG) Abnormalities that are new and/or normalize on recovery (must have all findings)
Diffuse concave-upward ST-segment elevation
ST-segment depression in aVR
PR-depression throughout the leads without reciprocal ST-segment changes
OR
Physical examination findings: at least 1 finding
Pericardial friction rub
Distant heart sounds (infant/children)
Pulsus paradoxus

Pericarditis Level of Certainty - 2 (Probable Case)
Clinical Symptoms
Clinical Cardiac Symptoms (at least 1 finding below)
Acute chest pain or pressure
Palpitations
Dyspnea after exercise, at rest, or lying down
Diaphoresis
Sudden death
OR
Infants/Children (at least 2 findings below)
Irritability
Vomiting
Poor feeding
Sweating
AND
Physical examination findings: (at least 1 findings)
Pericardial friction rub
Pulsus paradoxus
OR
Evidence of abnormal fluid collection or pericardial inflammation by imaging (Echo, MR, cMR, CT)
OR
Electrocardiogram (EKG) Abnormalities that are new and/or normalize on recovery (at least 1 finding below)
Diffuse concave-upward ST-segment elevation
ST-segment depression in aVR
PR-depression throughout the leads without reciprocal ST-segment changes
AND
No alternative diagnosis for symptoms (e.g. MI, PE, mediastinitis, etc)

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Pericarditis Level of Certainty - 3 (Possible Case)

Clinical Symptoms

Clinical Cardiac symptoms (at least 1 finding below)

- New onset cardiac chest pain or pressure
- Palpitations
- Dyspnea after exercise, at rest, or lying down

AND

Non-Specific Symptoms (at least 1 finding below)

- Cough
- Weakness
- Gastrointestinal - nausea, vomiting diarrhea
- Shoulder/upper back pain
- Cyanosis
- Low grade intermittent fever
- Altered Mental Status
- Edema
- Fatigue

OR

Infants/Children (at least 2 findings below)

- Irritability
- Vomiting
- Poor feeding
- Back Pain
- Tachypnea
- Lethargy

AND

Abnormal testing

Abnormal chest radiograph showing enlarged heart

OR

Electrocardiogram (EKG) abnormalities

- Non-specific changes that are new and/or normalize in recovery

AND

No alternative diagnosis for symptoms (e.g. MI, PE, mediastinitis, etc)

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Supplementary table 3: Myocarditis Brighton Collaboration case definition

Myocarditis Level of Certainty - 1 (Definitive Case)
Histopathologic examination of myocardial tissue (autopsy or endomyocardial biopsy) showed myocardial inflammation
OR
Elevated myocardial biomarkers (at least 1 of the findings below)
Troponin T
Troponin I
AND
Abnormal Imaging study
Abnormal Cardiac Magnetic Resonance Study (at least 1 of the findings below)
Edema on T2 weighted study, typically patchy in nature
Late gadolinium enhancement on T1 weighted study with an increased enhancement ratio between myocardial and skeletal muscle typically involving at least one non-ischemic regional distribution with recovery (myocyte injury).
OR
Abnormal Echocardiogram (at least 1 of the findings below)
New focal or difuse left or right ventricular function abnormalities (eg. decreased ejection fraction)
Segmental wall motion abnormalities
Global systolic or diastolic function depression/abnormality
Ventricular dilation
Wall thickness change
Intracavitary thrombi

Myocarditis Level of Certainty - 2 (Probable Case)
Clinical Symptoms
Cardiac Symptoms (at least 1 finding below)
Acute chest pain or pressure
Palpitations
Dyspnea after exercise, at rest, or lying down
Diaphoresis
Sudden death
OR
Non-Specific Symptoms (at least 2 findings below)
Fatigue
Abdominal pain
Dizziness/syncope
Edema
Cough
OR
Infants and young children (at least 2 findings below)
Irritability
Vomiting
Poor feeding
Tachypnea
Lethargy
AND
Testing supporting diagnosis (Biomarkers, ECHO, and EKG)
Elevated myocardial biomarkers (at least 1 of the findings below)
Troponin T
Troponin I
CK Myocardial band
OR

- Echocardiogram (ECHO) abnormalities (at least 1 of the findings below)
  - New focal or difuse left or right ventricular function abnormalities (eg. decreased ejection fraction)
  - Segmental wall motion abnormalities
  - Global systolic or diastolic function depression/abnormality
  - Ventricular dilation
  - Wall thickness change
  - Intracavitary thrombi
- OR
- Electrocardiogram (EKG) abnormalities that are new and/or normalize on recovery(at least 1 of the findings below)
  - Paroxysmal or sustained atrial or ventricular arrhythmias (premature atrial or ventricular beats, and/or supraventricular or ventricular tachycardia, interventricular conduction delay, abnormal Q waves, low voltages)
  - AV nodal conduction delays or intraventricular conduction defects (atrioventricular block (grade I-III), new bundle branch block)
  - Continuous ambulatory electrocardiographic monitoring that detects frequent atrial or ventricular ectopy
- AND
- No alternative diagnosis for symptoms

Myocarditis Level of Certainty - 3 (Possible Case)

- Clinical Symptoms
  - Cardiac symptoms (at least 1 finding below)
    - Acute chest pain or pressure
    - Palpitations
    - Dyspnea after exercise, at rest, or lying down
    - Diaphoresis
    - Sudden death
  - OR
  - Non-Specific Symptoms (at least 2 findings below)
    - Fatigue
    - Abdominal pain
    - Dizziness/syncope
    - Edema
    - Cough
  - OR
  - Infants/Young children (at least 2 findings below)
    - Irritability
    - Vomiting
    - Poor feeding
    - Tachypnea
    - Lethargy
- AND
- Biomarkers supporting evidence of inflammation (at least 1 finding below)
  - Elevated CRP
  - Elevated ESR
  - Elevated D-Dimer
- AND
- Non-Specific Electrocardiogram (EKG) Abnormalities that are new and/or normalize on recovery (at least 1 finding below)
  - ST-segment or T-wave abnormalities (elevation or inversion)
  - PACs and PVCs
- AND
- No alternative diagnosis for symptoms

Box 1: Expanded investigation to consider in the investigation of select cases of myocarditis / pericarditis

These investigations may be sent in consultation with infectious diseases, cardiology and rheumatology. Other investigations may be required as deemed appropriate and based on exposure history.

- **Blood lab:**
  - CBC & differential, CRP, blood gas, lactate, glucose, creatinine, urea, albumin
  - Calcium total, ionized calcium, magnesium, copper, selenium, ammonium
  - Bilirubin (conjugated/unconjugated), alkaline phosphatase, ALT, GGT, AST
  - CK, NT-proBNP
  - Cholesterol, 25-Hydroxyvitamin D, TSH
  - Acylcarnitines, anti-nuclear antibody, ASOT, DNA banking
- **Viral serologies:**
  - Mycoplasma pneumoniae IgM antibody
  - Parvovirus B19 IgG & IgM
  - EBV serology
  - CMV IgG and IgM
  - Toxoplasma serology
  - Bartonella serology (as applicable, depending on exposure history)
  - HIV serology (depending on risk factors)
- **Other microbiological testing**:
  - Blood enterovirus PCR
  - Blood HSV/VZV PCR
  - Blood Adenovirus quantitative PCR
  - Blood parvovirus B19 PCR
  - Blood CMV/EBV/HHV6 PCR
  - Nasopharyngeal swab for respiratory virus multiplex PCR
  - Throat bacterial culture
  - Throat mycoplasma/Chlamydophila pneumoniae PCR
  - Stool (GI) multiplex PCR and enterovirus PCR
  - Tuberculin skin test (TST) or IGRA (as applicable, depending on exposure history)

* Please refer to the EPIC order set for myocarditis

For additional information on myocarditis and pericarditis following COVID-19 mRNA vaccination and other useful documents, please visit the following links:

Public Health Ontario Ontario AEFI reporting form: https://www.publichealthontario.ca/-/media/documents/a/2020/aefi-reporting-form.pdf?la=en

Adverse events following COVID-19 immunization in Ontario (Public Health Ontario): https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-aefi-report.pdf?la=en.

2015 ESC Guidelines for the diagnosis and management of pericardial diseases (European Society of Cardiology): https://academic.oup.com/eurheartj/article/36/42/2921/2293375

Diagnosis and Treatment of Myocarditis in Children in the Current Era (American Heart Association): https://www.ahajournals.org/doi/10.1161/circulationaha.113.001372

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