

## Editorial

**Cite this article:** Fremed MA, Lytrivi ID, Liberman L, Anderson BR, Barry OM, Choudhury TA, Chrisomalis-Dring S, Ferris A, Glickstein JS, Krishnan U, Levasseur S, Rosenzweig EB, Shah A, Silver ES, Suh S, Turner ME, Weller R, Woo J, and Starc TJ (2020) Cardiac workup and monitoring in hospitalised children with COVID-19. *Cardiology in the Young* 30: 907–910. doi: [10.1017/S1047951120001778](https://doi.org/10.1017/S1047951120001778)

Received: 29 May 2020



Revised: 1 June 2020

Accepted: 1 June 2020

First published online: 2 July 2020

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# Cardiac workup and monitoring in hospitalised children with COVID-19

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## Abstract

Approximately, 1.7 million individuals in the United States have been infected with SARS-CoV-2, the virus responsible for the novel coronavirus disease-2019 (COVID-19). This has disproportionately impacted adults, but many children have been infected and hospitalised as well. To date, there is not much information published addressing the cardiac workup and monitoring of children with COVID-19. Here, we share the approach to the cardiac workup and monitoring utilised at a large congenital heart centre in New York City, the epicentre of the COVID-19 pandemic in the United States.

SARS-CoV-2, the virus responsible for the novel coronavirus disease-2019 (COVID-19), has infected millions of individuals worldwide with approximately 1.7 million infections in the United States at the time of writing.<sup>1</sup> A growing body of literature has described cardiac manifestations of this disease in adults, including myocarditis and arrhythmias,<sup>2,3</sup> electrocardiographic changes including ST segment elevations, T wave inversions, and laboratory abnormalities such as elevated high-sensitivity troponin T and N-terminal pro-brain-type natriuretic peptide. Although the pathophysiology is unclear, these abnormalities are associated with increased morbidity, such as need for intubation, and mortality.<sup>4–8</sup> Adults have been disproportionately affected, with children making up under 3% of the infected population.<sup>1,9</sup> Given the smaller numbers of paediatric cases, there is a paucity of cardiac data available.

While recommendations have been published with regards to general paediatrics,<sup>10</sup> paediatric cardiac catheterisation,<sup>11</sup> cardiothoracic surgery,<sup>12</sup> and pulmonary hypertension,<sup>13,14</sup> there remains a lack of consensus guidelines for non-interventional cardiac workup and monitoring of children hospitalised with COVID-19. In this report, we share our approach to the cardiac workup and monitoring of these children with regards to laboratory, electrocardiographic, and imaging evaluation of children with respiratory presentations of COVID-19 with the goal of increasing awareness of the cardiac manifestations of this disease, suggested diagnostic tests, and when to call the paediatric cardiologist. This was based on our experience at a major congenital heart centre in New York City, the epicentre of the COVID-19 pandemic in the United States. During this time, all paediatric admissions to NewYork-Presbyterian Hospital system sites across New York City were consolidated at Morgan Stanley Children's Hospital. Recently, groups have reported children with COVID-19, or exposure to close contacts with COVID-19, who develop a multi-system inflammatory syndrome.<sup>15,16</sup> The protocols outlined here are intended for application to acute presentation of the “classic” respiratory presentation of COVID-19. Our institution is currently developing a separate multidisciplinary protocol detailing our approach to this new entity, which will be submitted for publication separately.

Criteria for admission at our institution include, but are not limited to, respiratory distress, supplemental oxygen requirement, cardiovascular instability, dehydration, or medications requiring inpatient monitoring. In deciding the appropriate workup, we consider suspicion for cardiac involvement and acuity level (Table 1).

## Children without suspicion for cardiac involvement

Patients with normal blood pressure and cardiac exam, absence of hepatosplenomegaly, normal cardiac size on chest X-ray, normal high-sensitivity troponin T and N-terminal pro-brain-type natriuretic peptide, and who do not meet criteria for multi-system inflammatory syndrome can be considered low risk for cardiac involvement. All children with confirmed or suspected COVID-19 should have basic laboratory studies drawn according to their institution specific protocol, but should include at least a complete blood count with differential, electrolytes, renal

**Table 1.** Cardiac workup and monitoring in children with and without suspicion for cardiac disease

Children without suspicion for cardiac disease	Children with suspicion for cardiac disease
<ul style="list-style-type: none"> <li>• <b>Baseline Labs:</b> as per institution protocol</li> <li>○ CBC with differential</li> <li>○ Chemistry</li> <li>○ ESR/CRP</li> <li>○ Ferritin</li> <li>○ Procalcitonin</li> <li>○ D-dimer</li> <li>○ Fibrinogen</li> <li>○ LDH</li> <li>○ IL-6</li> <li>• <b>Additional cardiac screening</b></li> <li>○ hs-Troponin T, once</li> <li>○ NT-proBNP, once</li> <li>• <b>15 Lead ECG IF:</b></li> <li>○ Starting potentially QTc prolonging medication</li> <li>○ Admitting to ICU</li> <li>• <b>Routine echocardiogram:</b> not recommended</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline Labs Plus:</b></li> <li>○ hs-Troponin T q24–72h</li> <li>○ NT-proBNP q24–72h</li> <li>• <b>Cardiac monitoring:</b> Assess arrhythmia burden</li> <li>• <b>15 Lead ECG to assess for:</b></li> <li>○ Myocarditis</li> <li>○ Rhythm disturbance</li> <li>○ Baseline QTc, T waves, and ST segments</li> <li>• <b>Echocardiogram: at discretion of cardiologist including:</b></li> <li>○ Ventricular function</li> <li>○ Valvar regurgitation</li> <li>○ Pericardial effusion</li> <li>○ Proximal coronary arteries</li> <li>○ Additional views if high suspicion of structural or congenital heart disease</li> </ul>

CBC = complete blood count; CRP = C-reactive protein; ECG = electrocardiogram; ESR = erythrocyte sedimentation rate; hs-Troponin T = high-sensitivity troponin T; IL-6 = interleukin 6; LDH = lactate dehydrogenase; NT-proBNP = N-terminal pro-brain-type natriuretic peptide

and liver function tests, erythrocyte sedimentation rate, and C-reactive protein. In addition, a screening high-sensitivity troponin T and N-terminal pro-brain-type natriuretic peptide should be measured in all admitted children. A chest X-ray is useful in assessing cardiac size, confirming clinically suspected pneumonia, and evaluating respiratory failure, and should be obtained for children admitted with COVID-19.

We do not obtain routine electrocardiograms or echocardiograms for children with acute respiratory presentations of COVID-19 without suspicion for cardiac disease given the added exposure to staff. However, an electrocardiogram should be obtained for patients requiring ICU admission, as well as prior to starting therapy with corrected QT interval (QTc) prolonging medications, such as hydroxychloroquine, azithromycin, and lopinavir/ritonavir,<sup>17</sup> regardless of suspicion for cardiac involvement. Because the QTc appears to achieve peak prolongation between days 3 and 4 of treatment<sup>18</sup> and hydroxychloroquine has a long half-life,<sup>19</sup> these patients should continue to have their QTc monitored after completing the medication course. Due to a recent study showing increased rates of arrhythmia and mortality with hydroxychloroquine use,<sup>20</sup> its role in the treatment of children with severe COVID-19 is unclear. However, since the impact of other experimental therapies such as remdesivir is not yet known, we suggest close monitoring of the QTc even in the absence of hydroxychloroquine use.

In cases where hydroxychloroquine is still being used, published recommendations suggest that the QTc should be less than 500 ms for patients with normal QRS durations and less than 520 ms for patients with prolonged QRS durations prior to initiating therapy. If the QTc is borderline (460–500 ms), treatment may be initiated with caution.<sup>18,21</sup>

More frequent monitoring of the QTc may be warranted in patients with comorbid conditions known to prolong the QTc, including congenital long QT syndrome, severe renal insufficiency,<sup>22</sup> treatment with other QTc prolonging medications, and

electrolyte disturbances such as hypokalaemia, hypomagnesemia, and hypocalcemia. Electrolyte abnormalities should be corrected prior to initiating QTc prolonging therapies and electrolytes should be closely monitored for the duration of therapy. Concurrent use of other QTc prolonging medications should be avoided.

### Children with suspicion or at risk for cardiac involvement

Growing evidence suggests common involvement of multiple organ systems including the heart, kidneys, and brain.<sup>23–26</sup> There are many situations for which the paediatric cardiology team might be consulted. These may include abnormal physical exam findings suggestive of heart failure, such as inappropriate tachycardia or arrhythmia, gallop, pericardial friction rub, or jugular venous distention, evidence of cardiogenic shock, or pulmonary hypertension. Elevated high-sensitivity troponin T or N-terminal pro-brain-type natriuretic peptide or cardiomegaly on chest X-ray also warrant a cardiology consult. The paediatric cardiologist may also be consulted for abnormal electrocardiogram, including changes associated with pericardial or myocardial inflammation.

Patients who are at risk for severe infection and may be more likely to require admission to the ICU include infants and those with underlying comorbidities such as lung disease, cardiovascular disease, chronic kidney disease, diabetes, and metabolic or immune disorders.<sup>27,28</sup> Based on consensus opinion at our institution, we suggest that special consideration should be given to patients with pulmonary hypertension, unrepaired complex congenital heart disease, cyanotic heart disease with oxygen saturations less than 85%, ventricular dysfunction requiring medical therapy, and history of heart transplantation on immunosuppressive medications. Due to their higher risk profile, these patients may warrant a more complete evaluation than those without pre-existing conditions.

### Laboratory studies

In accordance with institutional COVID-19 protocol, children with confirmed or suspected acute COVID-19 requiring admission undergo laboratory workup including complete blood count, chemistry, inflammatory markers, high-sensitivity troponin T, and N-terminal pro-brain-type natriuretic peptide. In our experience, for children with suspected cardiac involvement, it is useful to trend high-sensitivity troponin T and N-terminal pro-brain-type natriuretic peptide every 24–72 hours. If these are grossly abnormal or continuing to rise, we obtain an electrocardiogram and echocardiogram and consider transfer to the ICU, if not already admitted there.

### Electrocardiography/reviewable cardiac monitoring

Children with suspicion for cardiac involvement or multi-system inflammatory syndrome should have a screening electrocardiogram to assess for myocarditis or arrhythmia and establish a baseline for QTcs, T waves, and ST segments. If the electrocardiogram has findings suggestive of ischaemia or inflammation, such as T-wave inversions or ST segment elevations or depressions, we suggest obtaining electrocardiograms daily until the abnormalities resolve or the clinical situation has improved. All patients with suspicion for cardiac involvement, as well as those admitted to the ICU, should be placed on reviewable cardiac monitoring to assess arrhythmia burden.

## Echocardiography

The decision to perform an echocardiogram is made at the discretion of the paediatric cardiologist based on clinical, laboratory, and electrocardiographic data, with careful consideration given to reducing viral exposure for staff in the setting of widespread infection. At our institution, we developed a protocol for focused studies, keeping in mind the following goals such as assess for signs of myocarditis or myocardial dysfunction, evaluate for evidence of pulmonary hypertension/pulmonary embolus, and minimise exposure to the sonographer. We suggest obtaining an echocardiogram for those children with suspicion for cardiac involvement, including those with physical examination findings concerning for heart failure, abnormal laboratory values or electrocardiograms with evidence of myocardial injury, or who present with multi-system inflammatory syndrome. Our current protocol includes assessment of ventricular function, valvar regurgitation, presence of pericardial effusion, and, with the newly described multi-system inflammatory syndrome in children<sup>15,16</sup> in mind, evaluation of the proximal coronary arteries in children with confirmed or suspected COVID-19 who require an echocardiogram. Children with known or suspected congenital heart disease should have a complete congenital transthoracic echocardiogram performed when necessary. In order to limit staff exposure, all measurements are done after the sonographer has left the patient room.

Although extracorporeal membrane oxygenation use appears to be infrequent in children with COVID-19,<sup>29</sup> there is evidence that it may provide a survival benefit for adults with severe infection,<sup>30</sup> though its use is not consistent across all centres.<sup>31</sup> In this situation, echocardiography may be required to assess cannula position, ventricular function, and presence of left atrial hypertension.

In our opinion, following hospital discharge, a complete follow-up echocardiogram is recommended in the out-patient setting for those children with abnormalities on the initial study. The optimal timing of follow-up has yet to be established and will be determined primarily by considering the clinical context as well as staff exposure and facility capacity in the setting of the evolving pandemic.

## Arrhythmia

Arrhythmia has been reported as a significant issue in adult patients with COVID-19<sup>2,3</sup> and may be secondary to myocardial injury or direct effects of cytokines on sodium and potassium channels.<sup>32</sup> Interleukin-6 has been shown to be elevated in those with myocardial injury compared with those without.<sup>33</sup> These same cytokines may also inhibit enzymes required for clearing certain QTc prolonging medications, thereby enhancing their impact on the QTc.<sup>31</sup> Other potential etiologies for arrhythmia include metabolic disturbance,<sup>34</sup> hypoxia,<sup>35</sup> and genetic dysrhythmias, which may be revealed by acute illness or significant stressors, such as Brugada syndrome<sup>36</sup> and long QT syndromes.<sup>37</sup> If there is an associated elevation in high-sensitivity troponin T, early myocarditis should be considered.<sup>38</sup> Due to the risk of arrhythmia, we suggest that these patients be placed on reviewable cardiac monitoring.

## Limitations

Significant limitations exist that may impact the relevance of this approach, most importantly that the practices outlined in this report are based primarily on expert opinion and adult literature rather than paediatric data. The number of children with COVID-19

worldwide is small relative to the number of adults and our understanding of it is evolving rapidly, resulting in relatively limited data addressing paediatric cardiac involvement. Prospective data collection is necessarily impeded by the need to minimise exposure of phlebotomy, electrocardiogram, and echocardiogram staff. Furthermore, the natural history and underlying pathophysiology of this disease in children, including the newly emerging multi-system inflammatory syndrome in children, is just now being described. These practices reflect our best understanding at the time of writing; however, our knowledge of this disease and its various presentations is constantly evolving and clinical practice must necessarily evolve in-kind.

## Conclusions

Providers caring for children with acute COVID-19 should keep cardiac involvement in mind and consult paediatric cardiology when there is suspicion for cardiac injury. In our opinion, the extent of workup and monitoring of these patients should be based on careful determination of clinical suspicion for cardiac disease and level of acuity of each patient, as well as the expected impact the information will have on clinical management. As the full picture of the multi-system inflammatory syndrome in children emerges, the role of the paediatric cardiologist will likely evolve and indications for testing may change. More information obtained from multi-centre collaboration is needed to establish definitive guidelines.

**Acknowledgements.** The authors acknowledge the contributions of the following members of the Columbia University Irving Medical Center Pediatric-Adult Congenital Heart Research Collaborative: Emile Bacha, Eva Cheung, Kanwal Farooqi, David Kalfa, Ganga Krishnamurthy, Matthew Lewis, Damien LaPar, Marlon Rosenbaum, and Julie Vincent.

**Financial Support.** Dr Anderson receives salary support from the National Institutes of Health/NHLBI (K23 HL133454).

**Conflicts of Interest.** None.

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