COVID-19 and acute heart failure: screening the critically ill

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There is a need to screen for acute heart failure in critically ill COVID-19 patients. Up to one-third of COVID-19 patients who are admitted to the ICU, albeit a select population, develop an acute cardiomyopathy [1], which could represent myocarditis or stress cardiomyopathy. Fulminant myocarditis has been identified as a cause of death in younger patients with Middle East Respiratory Syndrome [2], and a similar trend may follow with COVID-19, even though younger age groups comprise only a small proportion of the overall COVID-19 deaths.

An elevated and/or increasing troponin level may serve as an indicator of patients developing COVID-19-related cardiomyopathy [3]. In these patients, an elevated troponin *can* indicate inflammatory myocarditis rather than myocardial infarction (either type I or type II). Other causes could be pulmonary emboli or right ventricular dysfunction. Retrospective studies from China show that over 50% of patients who died from COVID-19 had evidence of heart failure, whilst nearly 60% had elevated biochemical markers consistent with acute cardiac injury [4].

In two separate cohort studies from Wuhan [3,5], the proportion of COVID-19 patients with evidence of cardiac injury [as defined by elevated levels of high sensitivity troponin (hsTn) with or without other biochemical markers] ranged from 20 to 28%. In both studies, patients with elevated hsTn were older and more likely to have a range of cardiovascular comorbidities including hypertension, diabetes, coronary artery disease and prior heart failure. In both studies, an elevated hsTn was associated with a marked increase in mortality: 50-60% in those with an elevated hsTn compared with a mortality rate of 5-10% for those who had a normal hsTn during hospitalisation. In addition, COVID-19 patients with elevated hsTn during admission experienced higher rates of acute respiratory distress syndrome (ARDS) necessitating higher rates of non-invasive and invasive ventilation, acute renal failure requiring renal replacement therapy and heart failure. A separate but related issue is that tachyarrhythmias (subtypes not known) occurred in 44% of COVID-19 patients who were hospitalised [6].

Whereas the mortality of the majority of older COVID-19 patients appears to be related to the development of multi-organ failure complicating ARDS [7, 8, 9], the cause of death in younger COVID-19 patients may be related to myocarditis [case report, 10]. This can develop when the pneumonitis itself is not clinically severe [11]. If it is a fulminant myocarditis, then where possible, these patients should be supported through this phase with mechanical support. The question remains as to what is the primary driver of this myocarditis – the virus or the host inflammatory response? The latter would seem more likely, particularly in younger patients, in keeping with an early and then delayed peak of a 'cytokine storm' [12].

We suggest the following algorithm to better identify COVID-19 patients at risk for severe heart failure and circulatory collapse, whilst balancing the need to protect health care workers from virus exposure and to preserve PPE:

1. Patients in the ED, who require hospital admission because of COVID-19 should have any prior history of heart failure or left ventricular impairment noted. Patients without chest pain should undergo usual investigations such as electrolytes, blood count, liver function tests, chest x-ray, as well as high sensitivity troponin (hsTn) and ECG. Patients with an elevated hsTn (greater than 99th centile for the assay) should be considered for telemetry, preferably in HDU/ICU. Useful adjunct tests include d-dimer, CRP, LDH, ferritin and BNP (or NT-proBNP) although the availability of the latter may vary between institutions. *If there are also* ECG changes (see below) then this should trigger a transthoracic echocardiogram (TTE) [13] with limited views (see below). Otherwise, a hsTn should be undertaken daily and an ECG second daily (see caveat below) in the

HDU/ICU. Although the literature for children is limited, we recommend that a child requiring hospitalisation for COVID-19 should have an ECG and troponin, and if these are abnormal, this should trigger a cardiac assessment which is likely to include a TTE.

2. For patients in the HDU/ICU/telemetry setting, an elevated hsTn (greater than 99th centile for the assay), which *continues to rise* (in the absence of chest pain) over three consecutive days with or without ECG changes (see below) should trigger a targeted TTE [13] (see below). Haemodynamic instability (e.g. increasing vasopressor requirement), *or* any inotropic requirement *or* clinical evidence of heart failure should be independent triggers for a targeted TTE.

   Two caveats to note:
   (i) If telemetry has the capability of interpolated ECG then this can be undertaken on a *daily* basis as there is no additional exposure to nursing staff. Characteristic ECG changes of significant LV dysfunction and/or myocarditis include: low QRS voltage consistent with myocardial oedema; occasionally LV hypertrophy if there is an underlying chronic cardiomyopathy (representative of increased LV mass); ST-segment elevation either global or in contiguous leads as seen in STEMI (see note below regarding myocardial infarction); ST-segment depression; T wave inversion (may be widespread); QRS widening (including LBBB) and PR-segment depression (pericarditis) [14].
   (ii) If there is evidence on telemetry of frequent ventricular ectopy and/or non-sustained VT, then this should trigger a TTE.

3. The following points are relevant when interpreting the LV appearance on TTE in the presence of an elevated and rising hsTn:

   (a) Normal or mildly increased LV size, with preserved or increased wall thickness, with global LV dysfunction (no regional wall motion abnormalities) suggests myocarditis rather than myocardial infarction.

   (b) Normal or mildly increased LV size with segmental wall motion abnormalities can occur in stress cardiomyopathy, myocarditis as well as myocardial infarction. Consideration of the diagnosis of myocardial infarction and its appropriate treatment should be made on a case-by-case basis. Fulminant myocarditis can display normal LV cavity size with severely impaired systolic function and thickened LV walls representing oedema [14].

   (c) Significant LV dilatation (e.g. LVEDD > 6.5cm) with significant LV dysfunction may suggest a pre-existing dilated cardiomyopathy, an underlying predisposition to a dilated cardiomyopathy exacerbated or precipitated by acute viral illness, or the rapid development of a *de novo* viral cardiomyopathy.

Therefore, a targeted (less than 10 mins) TTE (so as to minimise operator exposure time) would aim for a minimum of 3 views:

1. Parasternal long axis
2. Short axis (papillary muscle level)
3. 4-chamber apical

Information gained *offline* (aside from the assessment of left ventricular systolic function) for each of these views (corresponding to the order above) would be:

1. Left ventricular end diastolic diameter and wall thickness.
2. Assessment of regional wall motion abnormalities and for pericardial effusion.
3. LV and RV size. If the RV is disproportionately large at the time of the study, then additional views/TR Doppler assessment to assess pulmonary pressure should be considered. Further investigation for pulmonary embolism (PE) should be considered on a case by case basis given the pro-coagulant state of these patients [4].

It is not only left ventricular systolic function that is important but also the left ventricular morphology and size, which in themselves are prognostic, particularly in these younger patients with acute heart failure. As indicated in the CSANZ Imaging COVID-19 position statement [13], TTE should be used judiciously to avoid unnecessary staff exposure, and all personal protective precautions be made available.

Patients who develop acute heart failure should be managed in an ICU environment according to established guidelines with the use of intravenous diuretics and inotropic/vasopressor support for those who develop hypotension. In patients with progressive cardiogenic shock, who fail to respond to inotropic support, consideration of mechanical circulatory support (e.g. VA ECMO or Impella) may be appropriate, however, this requires careful evaluation of the overall clinical picture. Given the potential risk posed to healthcare staff from aerosol generation during high-flow nasal oxygen, non-invasive ventilation or positive pressure ventilation without an adequate seal, institutional/ departmental preparation is required for the management of acute respiratory failure (*Brewster DJ et al. Med J Aust 2020-in press*).

The underlying pathophysiology in these critically ill patients is a likely fulminant myocarditis, so consideration should be given for therapies such as high dose corticosteroids, intravenous immunoglobulin and even selective cytokine blockade that target hyperinflammation [15], although these are not yet proven. Novel markers of inflammation and emerging therapies should also be considered as the evidence comes to hand.

While endomyocardial biopsy is considered the 'gold standard' for diagnosis of acute myocarditis, experience with this procedure in Covid-19 patients is extremely limited. Isolated case reports have suggested that the findings on endomyocardial biopsy are non-specific and are non-contributory to patient management. Furthermore, the procedure carries risks for both the patient and proceduralist. Based on these considerations endomyocardial biopsy is not recommended.

We recommend that inpatient cardiac MRI should also be avoided as the risks of the prolonged scan time and magnet contamination are substantial and immediate management is unlikely to be changed by its use.

Some of these critically ill patients, particularly those with severe respiratory failure, may have RV dysfunction and potentially acute cor pulmonale (similar to acute PE) even without clinical evidence of pulmonary vascular thrombosis. Consequently, they may have an elevated troponin stemming from the right ventricle, which is an aspect that needs to be explored. This may trigger additional modifications to ventilatory management (e.g. PEEP titration).

The over-riding imperative in these critically unwell patients is that cardiac involvement, including myocarditis and cardiomyopathy, needs to be considered early and even after the acute respiratory phase is passing. Vigilance is required to identify and treat these patients.

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Adult pathway to screen for acute heart failure in COVID-19 patients admitted to hospital