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Cardiac MR in times of COVID-19

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Coronavirus (COVID-19) is a disease caused by a novel virus, SARS-CoV-2, where SARS stands for severe acute respiratory syndrome. Although this is not the first variant of a coronavirus – both SARS and MERS were prior coronaviruses that underwent animal to human transition – COVID-19 does appear to be more contagious than its predecessors or the typical influenza virus.

Many people infected with COVID-19 are asymptomatic. However, certain populations are at a substantially higher risk, including the elderly (over 65 years old) and those with immunosuppression and pre-existing lung and cardiovascular disease¹. Obesity also appears to be a particularly strong risk factor.

Historically, in terms of deaths there have been larger pandemics including the 40-50 million people who died from the Spanish flu of 1918-1919 and the ongoing AIDS/HIV epidemic that has killed up to 35 million people since 1981. We don't yet know the full impact COVID-19 will have on our society, economy and healthcare. The brutality of how the pandemic flooded certain countries led to partial collapses of regional healthcare systems. This is why it is important to think about how to address this pandemic. Countries such as Australia, Austria, South Korea and Norway that responded very quickly with lockdowns

to reduce the spread of the virus did better in terms of overall death rates². It appears, for the time being, that earlier restrictions had a positive impact on community spread and mortality, while a final evaluation of different strategies will not be possible for at least another year.

During the ongoing COVID pandemic, people are also dying from other causes because they either are afraid of going to emergency rooms or because some hospitals are overwhelmed with COVID-19 patients. In New York City, a severely affected region, there are excess deaths not attributed to COVID-19, including patients who are waiting for urgent interventions they cannot receive³. Furthermore, the pandemic is already having a significant impact on the US economy, leading to an unprecedented spike in unemployment and downstream effects that will affect society for several years.

COVID-19 impact on the cardiovascular system

The SARS-CoV-2 virus enters the body's cells through the angiotensin converting enzyme 2 (ACE2) receptor that is involved in regulating blood pressure and the vascular permeability, and that is especially

prevalent in the lungs and heart. After an incubation period of four to six days, typical symptoms such as sore throat, dry cough, fever, myalgia and loss of smell and/or taste occur. Not all COVID-19 positive patients will experience each of these symptoms, whereas fever, cough and a sore throat are frequent.

The first symptom of severe disease, often 4-6 days after the first clinical signs, is dyspnea (shortness of breath). COVID-19 can lead to extensive, necrotic inflammation in the lungs, associated with a poor prognosis. Recent findings suggest that SARS-CoV-2 infection causes endotheliitis in several organs that may cause a massive inflammatory response leading to local formation of blood clots⁴. Resulting pulmonary embolism may explain why people with COVID-19 experience a sudden deterioration of their respiratory function. Another aspect of this virus is the potential for increased permeability of the blood vessels through the ACE2 receptor leading to an escalation in edema.

The disease progresses in three pathological stages: infection, pulmonary phase and severe

disease caused by hyperinflammation⁵. In the first phase, viral infiltration and replication occurs with lymphocytopenia, a key laboratory finding. As the disease advances to the pulmonary phase, patients experience respiratory compromise and abnormal chest imaging. In the third and most severe phase, massive inflammation typically leads to extensive pulmonary damage with a subsequent lack of oxygen and finally multiorgan failure⁵.

This very strong response by the immune system has also been called the cytokine storm and it may initiate more damage than the virus itself, causing some of the young COVID-19 patients to be severely affected.

A high incidence of acute myocardial injury, likely around 20 percent, is associated with poor prognosis and therefore a potential target for aggressive treatment⁶. According to early reports, up to 50 percent of COVID-19 patients with acute myocardial injury may die⁶.

Elevated biomarkers such as troponin and clinical symptoms including arrhythmia, palpitations, heart failure and sudden death indicate acute myocardial injury. Acute coronary syndrome involving the coronary

arteries can lead to ischemic injury or an ischemic event such as myocardial infarction.

A consensus paper from the Society for Cardiovascular Angiography and Interventions (SCAI), American College of Cardiology (ACC) and the American College of Emergency Physicians (ACEP) recommend additional noninvasive evaluation in patients with an unclear or unequivocal diagnosis. Potential causes for myocardial injury can be ST-elevation myocardial infarction (STEMI), viral invasion itself, the inflammatory response of an overly active immune system or a mismatch systemic of oxygen supply and demand⁷. Therefore, if there is evidence of myocardial injury without a known etiology, more information is needed for informed clinical decision-making. Among various non-invasive diagnostic procedures, cardiac MR (CMR) has a unique potential.

Using CMR in COVID-19

CMR imaging enables the visualization of anatomy, function and tissue pathology. Reports on myocardial injury in patients with COVID-19 are still scarce, with one case of ischemic injury with involvement of a coronary artery⁸, and another with acute myocardial injury that was apparently caused by a direct inflammatory response and not an underlying coronary artery issue. In the latter case, T2 maps (from CMR) depicted evidence of pericardial

effusion in the pericardial sac. In the short axis view of the left ventricle, there was evidence of myocardial edema as indicated by increased T2 times of the more apical myocardium as well as the bright area indicative of increased water content consistent with myocardial edema as depicted in a PS MDE sequence in a four-chamber view⁹. A very recent case report confirmed this pattern¹⁰.

Because of its versatility, CMR is the technique of choice for a comprehensive assessment of the heart, specifically with respect to visualizing tissue pathology and thus specifically verifying or refuting the underlying cause of cardiac disease. It can help identify ischemic versus non-ischemic injury, where ischemic injury always involves the subendocardial layer while non-ischemic rarely does¹¹. Regional distribution of the injury also indicates ischemic or non-ischemic injury; there are certain patterns, that most often provide specific additional information on the origin of the injury¹², such as cardiomyopathies or certain infiltrative diseases.

Figure 1 shows a case of acute myocardial inflammation in a patient with COVID-19.

Except for very few diseases – sarcoid and myocarditis – the underlying cause of myocardial injury can generally be identified by the regional distribution.

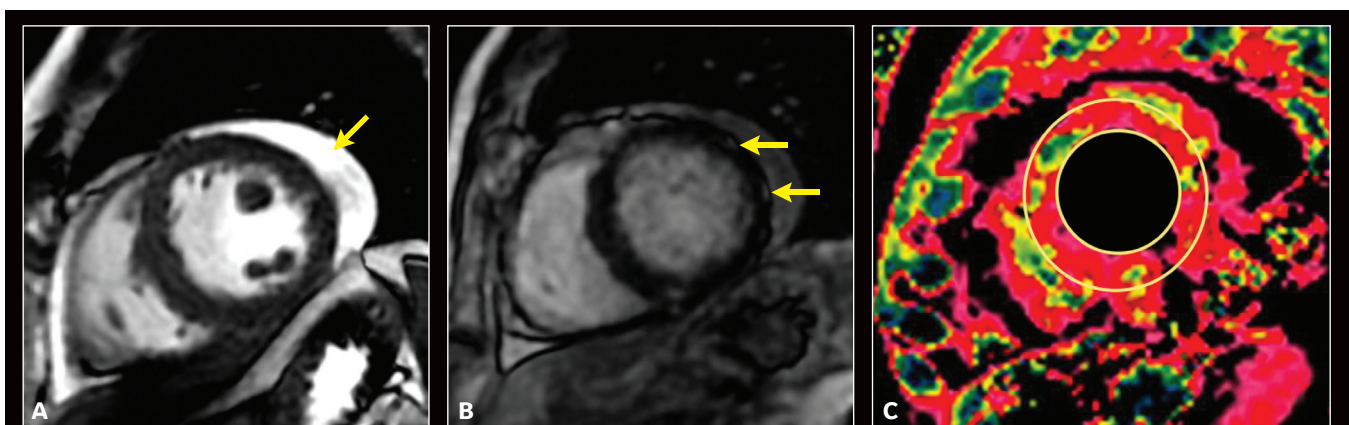


Figure 1. CMR findings in short axis views of a patient with COVID-19 related acute myocarditis. (A) Cine image with pericardial effusion (arrow); (B) late enhancement (MDE) image with mild patchy inflammatory necrosis (arrows); (C) T2 map showing increased T2 values (in red) for the entire LV myocardium, consistent with widespread myocardial edema. The LV volume was small and the resulting cardiac output reduced, despite tachycardia.

Among them, myocarditis (inflammation of the heart muscle) can be identified quite specifically with CMR using a combination of CMR “sequences” (protocol components), including mapping, cine imaging and late enhancement (MDE).

MDE imaging requires the administration of a contrast agent and can detect irreversible myocardial injury such as, necrosis, infiltration, or fibrosis/scars. The Lake Louise Criteria for the assessment of patients with suspected myocardial inflammation provides CMR protocol standards, and diagnostic criteria for identifying myocarditis¹³. There are main criteria for edema/acute inflammation (based on T2 as a water-sensitive marker that can be measured in CMR images) and irreversible myocardial injury in a non-ischemic regional distribution pattern. Supportive criteria include pericardial effusion and systolic left ventricular dysfunction¹⁴.

Safety of CMR in COVID-19 patients

CMR is considered the noninvasive gold standard for verifying or refuting a diagnosis of acute myocarditis. In COVID-19 patients, it's not just the accuracy of the technique; it's also keeping the healthcare staff safe. The virus is transmitted through the endothelium, particularly the mouth, nose and eyes. Transmission occurs through droplets and contaminated surfaces. Longer distance aerosol transmission of one to two meters is possible if enough of the virus droplets are in the air and six to eight meters around infected persons who are sneezing and coughing. The World Health Organization recommends at least 3 feet and the Centers for Disease Control and Prevention suggests 6 feet for safe social distancing^{15,16}.

It seems apparent that many of the countries with severe sudden outbreaks of COVID-19 are the result of mass

gatherings that served as a catalyst for rapid spreading: a mass religious gathering in South Korea; carnival in Germany; and beach parties in Italy and Florida. Therefore, if the healthcare staff has to work in a confined space without sufficient air filtering, the high risk is quite obvious.

While an MR exam does not generate the same risk for patient aerosols that intubation or resuscitation do, there is the risk that all patients can be carriers even those who are asymptomatic or have a negative test.

Therefore, during a pandemic, all patients should be considered as potential virus carriers. Accordingly, all staff members associated with the scan should have proper training in donning and doffing, as well as sufficient personal protective equipment (PPE).

Given the increased risk, surgical masks are not sufficient to efficiently protect the healthcare worker and therefore N95/FFP2 masks, face shields or protective glasses, gloves and an impermeable gown should be used in the presence of COVID-19 positive patients.

There are a few additional important considerations. A focused CMR protocol that reduces the time a patient is in the scanner should be utilized to reduce the risk of droplets in the scanner bore. Non-contrast scans that don't require an IV should be used when possible to avoid close contact with the patient and the risk of droplets. After the scan, it is important to carefully clean all surfaces that have been potentially contaminated, similar to the extended cleaning protocols that exist in many facilities with critically ill or intubated patients. Leaving the scanner room empty for 30 minutes after an exam allows for proper ventilation.

Clinical MR workflow

COVID-19 patients with a clinical suspicion of acute myocardial injury should be frequently (every 24 to 48 hours) checked for ST elevation in ECG, shortness of breath not otherwise explained, arrhythmia or atypical chest pain. Troponin, a sensitive serologic marker, should be measured in all patients with suspected acute myocardial injury. If troponin is elevated, a cardiac MR scan can differentiate normal from acute non-ischemic injury. Furthermore, it can also differentiate between numerous non-ischemic myocardial diseases.

CMR has been shown to have a strong impact on clinical decision making, such as whether the patient goes to cardiac catheterization or receives aggressive heart failure treatment, and, therefore, also on patient outcomes¹⁷.

If the heart appears relatively normal on CMR then further diagnostic testing for other underlying causes, e.g., lung injury, is warranted. The Society for Cardiac Magnetic Resonance (SCMR) has published recommendations for the use of CMR during the COVID-19 pandemic¹⁸.

One additional, important aspect regarding the use of MR in COVID-19 patients is that it can be used to examine other organs. In an unpublished case report of a patient in Iran undergoing an MR for breast disease, pulmonary findings consistent with COVID-19 were detected. Peripheral inflammation in the right lung was depicted in the T2-weighted images. The patient subsequently tested positive and developed moderate symptoms. This case indicates that in one scan, MR could double rule-out both pulmonary and cardiac involvement without the use of contrast. Although CT angiography has

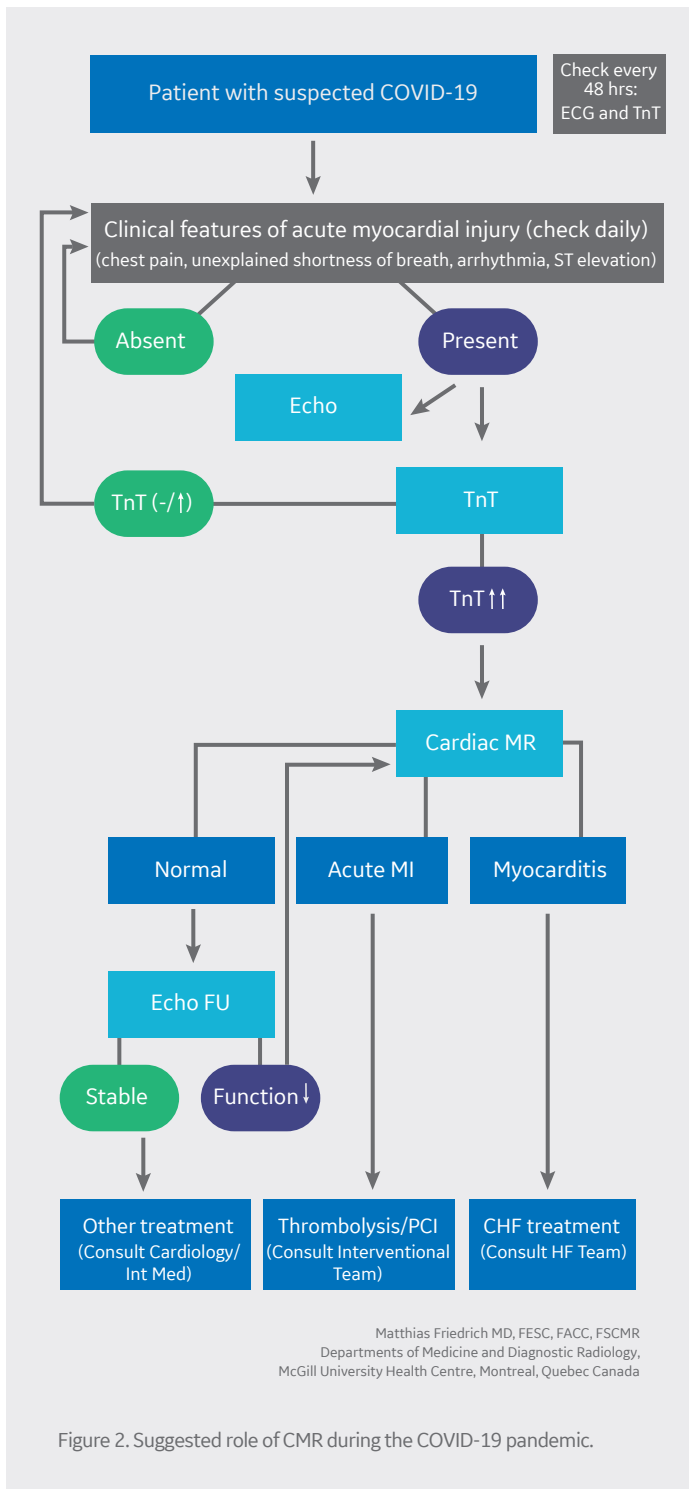


Figure 2. Suggested role of CMR during the COVID-19 pandemic.

a higher spatial resolution, this case illustrates that with a cardiac MR scan the clinician can examine both the lungs and the heart and avoid a separate CT scan, avoid another transport through the hospital and possibly save precious therapeutic decision-making time.

To summarize, CMR can play a critically important role in the workup of COVID-19 patients with signs of acute myocardial injury. Further, it can be combined with T2-weighted lung sequences as a double rule-out of myocardial and pulmonary injury and thus render CMR the role of a fast, highly efficient exam in all patients with suspected COVID-19. The safety of technologists should be ensured by proper training and availability of adequate PPE. **S**

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