

Application of Point-of-care Cardiac Ultrasonography in COVID-19 Infection: Lessons Learned from the Early Experience

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Abstract

The outbreak of the SARS-CoV-2 infection, also known as coronavirus disease 2019 (COVID-19), was formally defined a pandemic by the World Health Organization (WHO) in March 2020, and is still a global health issue. Since there is a high prevalence of acute cardiac injury in patients with COVID-19 infection, point-of-care cardiac ultrasound (PoCCUS) may be used for longitudinal monitoring of patients infected with COVID-19. However, there is still limited experience on the application of PoCCUS in the COVID-19 pandemic. Within the point of care setting in our system, focused cardiac US exams were performed with specific imaging protocols on the basis of suspicion of a specific disease, such as ruling out tamponade or thrombotic complications. Our preliminary experience shows that PoCCUS helps distinguish the causes of dyspnea in febrile patients. The COVID-19 infection may play a role in unmasking or exacerbating underlying chronic cardiovascular conditions, especially in patients with inadequate past history. In hospitalized patients with COVID-19, CURB-65 score for pneumonia severity and raised D-dimer were significantly associated with deep vein thrombosis (DVT). COVID-19 patients with DVT had worse prognosis, and patients with lower leg edema deserve further evaluation by using point-of-care ultrasound for the lower legs and heart. In COVID-19 patients with arrhythmia, PoCCUS used by experienced hands may reveal abnormal right ventricle (RV) functional parameters and lead to a more comprehensive cardiac US study. When there is suspicion of cardiac disease, PoCCUS can be done first, and if information is inadequate, limited transthoracic echocardiography (TTE), and critical care echocardiography (CCE) can be followed. Ultrasound practitioners should follow the standard precautions for COVID-19 as outlined by the Centers for Disease Control and Prevention to prevent transmission of infection, regardless of suspected or confirmed COVID-19.

Keywords: Arrhythmia, COVID-19, Deep vein thrombosis, Echocardiography, Focused cardiac ultrasound, Limited transthoracic echocardiography, Point-of-care ultrasound, Right ventricular function, SARS-CoV-2, Wireless hand-carried ultrasound

INTRODUCTION

The World Health Organization issued a public health emergency of international concern alarm on January 30, 2020^[1] and formally declared the SARS-CoV-2 also known as coronavirus disease 2019 (COVID-19) outbreak, a pandemic, on March 11, 2020.^[2] The current COVID-19 pandemic caused

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by novel coronavirus is burdening health-care providers around the world with massive demands for tests, diagnosis, and treatment.^[3] The way that health-care facilities operate globally has been thus strongly impacted.

Since ultrasonography (US) is a safe and widely used diagnostic tool in a variety of medical conditions and patient care, the current point-of-care ultrasound (PoCUS) device, with its miniature characteristics, is now easily available for bedside studies. Bedside lung and cardiac US examinations have been invaluable in the critically ill.^[4,5] PoCUS may, therefore, play a certain role during the COVID-19 pandemic.^[6] COVID-19 is associated with high contagiousness; furthermore, unstable patients with hypoxemia and hemodynamic failure carry significant risk at transportation. Chest computed tomography (CT), although being a sensitive modality in the evaluation of COVID-19 pneumonia,^[7] is a limited option for patients with suspected or established COVID-19.^[8] Lung US may provide certain important information similar to chest CT and superior to standard chest radiography for evaluation of pneumonia and/or adult respiratory distress syndrome (ARDS).^[9] Peng, *et al.* summarized their early experience with lung US for evaluation of COVID-19 in China. They described the US features occurred in a continuum from mild alveolar interstitial pattern, to severe bilateral interstitial pattern, and finally to lung consolidation in patients with COVID-19 respiratory disease in comparison with chest CT findings. They suggested that lung US has major utility for the management of COVID-19 with respiratory involvement due to its safety, repeatability, absence of radiation, low cost, and point-of-care use. Chest CT may be reserved for cases where lung US is not sufficient to answer the clinical question.^[8] Furthermore, chest US may be used for longitudinal monitoring of affected patients.^[8] Cardiac US is increasingly used within the point of care setting, as other advanced imaging modalities, such as CT, are not often available in the emergency department and almost impossible in the intensive care unit (ICU).^[10] Point-of-care cardiac ultrasound (PoCCUS) may also be used for longitudinal monitoring of affected patients. However, there is still limited experience on the application of PoCCUS in the COVID-19 pandemic. We, herein, report our preliminary experience and indicate some learning points to help fill a gap in knowledge of PoCCUS in the COVID-19 pandemic scenario.

CARDIAC INVOLVEMENT IN CORONAVIRUS DISEASE 2019 INFECTION

Since there is no validated treatment for COVID-19 so far, the main strategies are symptomatic and supportive care, such as keeping vital signs, maintaining oxygen saturation and blood pressure, and treating complications, such as secondary infections or organ failure.^[3] In a review of 235 hospitalized patients (mean age: 66 years) confirmed with COVID-19 infection in Union Hospital, Wuhan, China, 98 patients (41.7%) were diagnosed to have acute cardiac injury. Among them, 56 patients (57.1%) died. Patients

with acute cardiac injury were commonly associated with comorbidities such as hypertension (52 out of 98, 53.1%) and preexisting cardiovascular diseases (27 patients, 27.6%) (Xie MX, unpublished data). Shao *et al.* reviewed 761 records of patients with severe COVID-19 in Wuhan and identified 151 patients who had an in-hospital cardiac arrest (IHCA) during a study period of 40 days. After exclusions, a total of 136 patients were resuscitated and documented using the Utstein template. Data from 136 patients showed that 119 (87.5%) patients had a respiratory cause for their cardiac arrest, and 113 (83.1%) were resuscitated in a general ward. The initial rhythm was asystole in 89.7%, pulseless electrical activity (PEA) in 4.4%, and shockable in 5.9%. Most patients with IHCA were monitored (93.4%) and most resuscitation (89%) was initiated within 1 min. The average length of hospital stay was 7 days and the time from illness onset to hospital admission was 10 days. They found the survival of patients with severe COVID-19 pneumonia who had an IHCA was poor.^[11] Due to the high incidence of acute cardiac injury as a complication of COVID-19 and high mortality rate in the hospitalized patients with acute cardiac injury, all hospitalized patients confirmed with COVID-19 having possible cardiac symptoms should be evaluated with cardiac US. PoCCUS is by all means the modality of choice in this scenario.

POINT-OF-CARE CARDIAC ULTRASOUND IN CORONAVIRUS DISEASE 2019

PoCCUS, limited transthoracic echocardiogram (TTE), and critical care echocardiography (CCE) all play important roles in the evaluation of cardiovascular complications associated with infection. Within the point-of-care setting in our system, PoCCUS was applied in the context of the American Society of Echocardiography (ASE) protocol for POCUS,^[12] ASE recommendations for TTE,^[13] or the ASE CCE and POCUS training recommendations.^[14] Focused examinations were performed with specific imaging protocols on the basis of suspicion of a specific disease (e.g., rule out tamponade or thrombotic complications). The examination was usually done for once, per disease, but more frequently, if there was any change in clinical status. The PoCCUS findings related to the diagnosis sought in protocol with optional quantification. At PoCCUS, some routine cardiac US study items can be abbreviated to provide only critical information. When needed, more quantitative data as per a limited TTE can be done. Patients undergoing mechanical ventilation can be examined in the supine position to avoid being kept in the decubitus position for prolonged periods of time. Image archiving and formal reporting were done in our system. The PoCCUS machines we used at our system included EPIQ 7C (Philips Medical Systems, Andover, MA, USA) equipped with L12-5/S5-1 probe; portable US scanner M9 (Mindray, Guangdong, China) equipped with L10-3 probe, or wireless hand-carry US machine LU700 (LeSONO, Leltek Inc., Taipei, Taiwan) equipped with L10-5 or C5-2, or LU710PA (LeSONO) equipped with PA4-1 probe.

LESSONS LEARNED FROM THE EARLY EXPERIENCE OF PoCCUS IN CORONAVIRUS DISEASE 2019

On the basis of our early experience in fighting against COVID-19 in our system, we summarize hereby some learning points as follows:

Febrile patients with dyspnea

Given the symptoms of fever and dyspnea, PoCCUS examination can be conducted for a rapid assessment of the

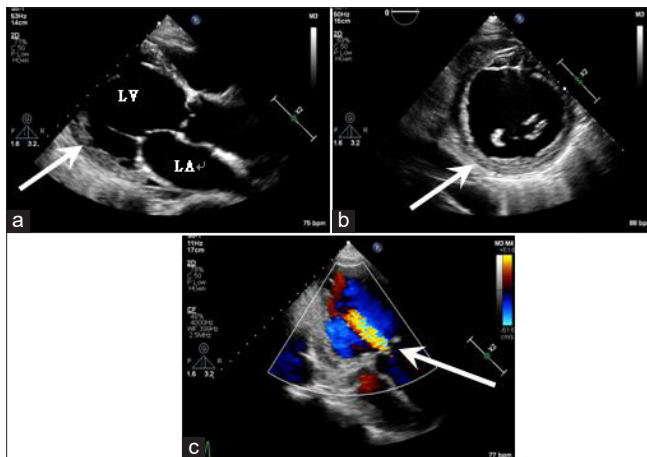


Figure 1: Point-of-care cardiac ultrasound shows (a and b) significantly enlarged left ventricle and left atrium, especially the left ventricle (arrow). Diffused weakening of the left ventricle wall motion is also noted. The patient was also noted to have coexisted aortic regurgitation which was not properly demonstrated during point-of-care cardiac ultrasound. (c) A subsequently comprehensive transthoracic echocardiogram at a later time revealed the coexisted aortic regurgitation (arrow). The left ventricular ejection fraction was 32%^[17]

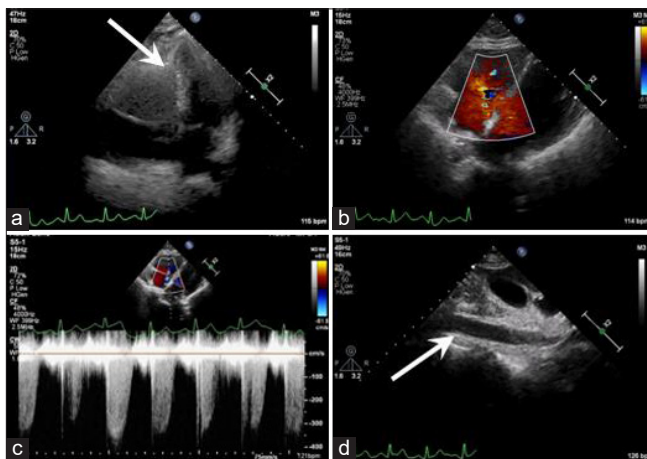


Figure 3: The right heart is enlarged on point-of-care cardiac ultrasound: (a) Apical 4-chamber view shows the ventricular septum (arrow) is deviated to the left ventricle. The right atrium is enlarged. (b) A subsequently comprehensive transthoracic echocardiogram reveals moderate tricuspid regurgitation. (c) Continuous-wave Doppler of the tricuspid valve demonstrates elevated regurgitant velocity consistent with increased pulmonary artery systolic pressure (with a pulmonary systolic pressure 74 mmHg). (d) Dilated inferior vena cava (arrow) (with the respiratory collapse rate <50%), suggesting increased right atrial pressure^[17]

left ventricular function. PoCCUS may assist in assessing the left ventricular function in cases of dilated cardiomyopathy and other causes of heart failure in a symptomatic patient with COVID-19. Dyspnea may be a sign of disease of the lungs or heart. The decision to perform cardiac US was mainly based on the symptoms and the finding of an elevated B-natriuretic peptide value which is known to be generally associated with an unfavorable course in heart failure and pneumonia.^[15,16] PoCCUS helps distinguish the causes of dyspnea. The COVID-19 infection, like many other acute inflammatory illnesses, may play a role in unmasking or exacerbating underlying chronic cardiovascular conditions, especially in patients with inadequate past history. Figures 1 and 2 demonstrate the usefulness of PoCCUS in unmasking the preexisting heart problems.^[17]

Lower leg edema, pleural effusion, and raised CURB-65 calculator or D-dimer level

Peripheral edema is often caused by heart failure, deep vein insufficiency, renal or liver diseases, low protein level, deep vein thrombosis (DVT), or infections. Obesity may predispose to edema.^[18] Peripheral edema may also occur in patients with severe systematic infection or septic shock under treatment

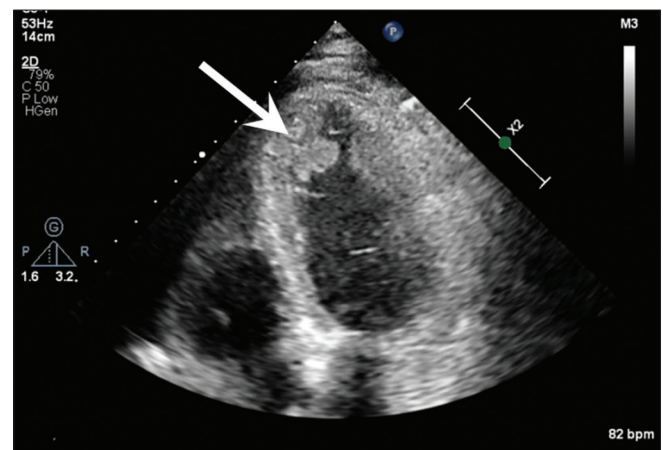


Figure 2: Apical 4-chamber view: Segmental wall motion abnormality with a large apical thrombosis (arrow) was noted^[17]

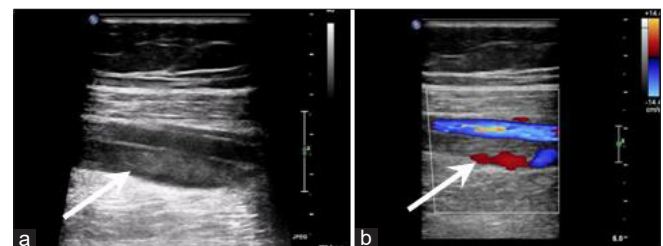


Figure 4: Gray-scale ultrasonography (a) and color Doppler ultrasonography (b) study of the veins of the lower extremity was performed. (a) Ultrasonography shows materials with heterogeneous echogenicity in the lumen of the posterior tibial vein which is distended (arrow), suggesting a newly formed thrombus. Color Doppler ultrasonography (b) shows a filling defect in the corresponding site. Obstruction of the flow is evident (arrow)

with fluid and electrolytes supply and monitoring. Both conditions are associated with a high mortality and morbidity. In a retrospective, multicenter cohort study, Zhou *et al.* enrolled 191 adult patients with COVID-19 and found that more than half of these patients developed sepsis.^[19] Early-goal-directed therapy has been shown to decrease in-hospital mortality and improve morbidity by decreasing the occurrence of severe organ dysfunction in septic patients.^[20] Pleural effusion is not a common finding in patients with COVID-19; however, pleural effusions and edema are commonly seen in critically ill patients with a reported prevalence of 62%^[21] and can be resulted from volume overload following aggressive fluid resuscitation.^[22] The diagnosis and management of pleural effusions in the intensive care or special COVID-19 units can be better guided and monitored using PoCCUS.

In our system, hospitalized patients with confirmed COVID-19 pneumonia were investigated for the presence of common complications, including DVT of lower extremities and ventricular dysfunction. Although ventricular dysfunction in patients with COVID-19 is rare, it can be vital for judging disease status and predicting outcomes [Figures 3 and 4]. In order to understand the clinical features and outcomes in the hospitalized COVID-19 pneumonia patients with DVT, we performed lower limb venous US within 1 month on 143 patients with confirmed COVID-19 pneumonia. Lower limb DVT was noted in 66 (46.2%) of these 143 patients (median time from the onset of illness to the detection of DVT was 21 days [interquartile range [IQR] 17–24]). Compared with non-DVT patients, patients with DVT were older, had lower oxygenation index, a higher rate of cardiac injury, and worse prognosis that included increased proportion of death (23 [34.8] vs. 9 [11.7], $P = 0.001$) and decreased proportion of discharge (32 [48.5] vs. 60 [77.9], $P < 0.001$). The multivariable logistic regression models to explore the risk factors of DVT showed that higher CURB-65 score was associated with DVT in patients with COVID-19 (CURB-65 score = 3–5, odds ratios = 6.122, 95% confidence interval [CI] = [1.190, 31.773], $P = 0.031$).^[23] The CURB-65 score can be used in the emergency or intensive care setting to risk stratify a patient's community-acquired pneumonia.^[24] The CURB-65 calculator has been highly recommended by the British Thoracic Society for the assessment of severity of pneumonia.^[25] On the basis of our study, we found that the prevalence of lower limb DVT is high and is associated with adverse outcomes in hospitalized patients with COVID-19. The CURB-65 calculator can provide information about the risk of DVT, and thus is recommended to be checked in hospitalized patients with COVID-19. Prophylaxis for venous thromboembolism may be protective in patients with a Padua protection score ≥ 4 after admission based on our study.

A more recent study from a single center in Amsterdam observed the cumulative incidence of symptomatic DVT in 75 patients positive for COVID-19, admitted to ICU, and receiving routine thromboprophylaxis. The incidence increased from 10% (95% CI, 5.8–16) at 7 days to 21% (95% CI, 14–30) at 14 days and 25% (95% CI 16–36) at 21 days.^[26]

In another study reviewing 81 COVID-19 patients in the ICU of Union Hospital, Tongji Medical College, China, Cui *et al.* found lower limb DVT in 20 patients, and 8 of them succumbed.^[27] Klok *et al.* reported 25 cases of pulmonary emboli among 184 COVID-19 patients in a Netherlands series with 18 involving at least segmental pulmonary arteries; in addition, they also noted three patients with venous thrombosis and 3 with strokes. They confirmed the very high ischemic cumulative incidence of thrombotic complications in critically ill patients with COVID-19 pneumonia.^[28]

Fibrin degradation results in an increase in circulating D-dimers and is a marker of infection and an expected feature of disseminated intravascular coagulation. In patients with COVID-19, plasma D-dimer concentration correlated with in-hospital mortality.^[28,29] In a French series of 107 patients, 22/107 patients developed pulmonary emboli, and the hazard ratio for pulmonary embolus increased with increasing D-dimer concentration.^[30] The increasingly strong evidence of venous thrombosis and pulmonary embolism in severely ill patients with COVID-19 has encouraged recommendations to use an anticoagulant in seriously ill patients, especially those with raised D-dimer concentrations.^[31]

Arrhythmia and right heart dysfunction in patients with Coronavirus Disease 2019

It has long been observed that virus infections can cause cardiac arrhythmia. A few studies investigated the effect of arrhythmia on the right ventricle (RV) function in viral pneumonia and the molecular mechanisms (such as coxsackie virus-adenovirus-receptor) have been discovered.^[32] As this global pandemic continues to rage, cardiovascular, especially arrhythmic, manifestations associated with COVID-19 have become evident.^[7,33] A report from Wuhan, China, noted that 16.7% of hospitalized and 44.4% of ICU patients with COVID-19 had arrhythmias.^[33] The presence of arrhythmia was noted to be an independent predictor of RV dysfunction in COVID-19. Elevation in cardiac troponin level is variable among hospitalized patients with COVID-19, with reported frequencies of 7% to 28%.^[7,34] In a global survey completed by 1197 respondents, Gopinathannair *et al.* reported that atrial fibrillation was the most commonly encountered tachyarrhythmia in COVID-19 patients, whereas severe sinus bradycardia and complete heart block were the most common brad arrhythmias. Ventricular tachycardia/ventricular fibrillation (VT/VF) arrest and PEA were reported by 4.8% and 5.6% of respondents, respectively.^[35] Guo *et al.* in a single-center retrospective study of 187 patients from Wuhan, China, evaluated the association of underlying cardiovascular disease and myocardial injury on fatal outcomes in patients with COVID-19. They noted that 28% of patients had myocardial injury as evidenced by elevated troponin T (TnT) levels. The incidence of VT/VF was 5.9% and increased to 17.3% in patients with elevated TnT.^[36] Recent literature has shown that cardiac troponin I (cTnI) concentration is only marginally increased in all COVID-19 patients, while values exceeding the 99th percentile in the upper reference limit can

only be observed in 8%–12% of positive cases.^[37] Nonetheless, what seems to emerge from the report of Lippi *et al.* is that cTnI values are significantly increased in their patients with severe SARS-CoV-2 (COVID-19) infection compared to those with milder forms of disease. It is, therefore, reasonable to hypothesize that initial measurement of cardiac damage biomarkers immediately after hospitalization for COVID-19, as well as longitudinal monitoring during hospital stay, may help identify a subset of patients with possible cardiac injury and thereby predict the progression of COVID-19 toward a worse clinical picture.^[38] In our recent study of 120 consecutive patients with COVID-19 who underwent echocardiography examination, we compared patients in the highest and the lowest RV longitudinal strain (RVLS) tertiles. We found that those in the lowest tertile were more likely to have a higher heart rate, D-dimer and C-reactive protein, high-flow oxygen and invasive mechanical ventilation therapy, higher incidence of acute heart injury, ARDS, DVT, and higher mortality. In this study, conventional RV functional parameters, including RV fractional area change, tricuspid annular plane systolic excursion, and tricuspid tissue Doppler annular velocity, were obtained. RVLS was determined using two-dimensional (2-D) speckle-tracking echocardiography. RV function was categorized in tertiles of RVLS. The study demonstrated that RVLS was a powerful predictor of higher mortality in patients with COVID-19 and supported that RVLS can be applied to identify higher risk COVID-19 patients.^[39]

PoCCUS is an abbreviated cardiac US study to provide only critical information. However, an experienced PoCCUS operator or echocardiasonographer may notice some abnormal RV functional parameters on 2-D US, and more quantitative data as per a limited TTE can be done subsequently, especially in COVID-19 patients with arrhythmia.^[39]

CONCLUSION

Lessons learned from the early experience of PoCCUS in COVID-19 highlighted that COVID-19 infection may mark or exacerbate underlying chronic cardiovascular conditions. Proper application of PoCCUS helps distinguish the causes of dyspnea in febrile patients, especially in patients with inadequate past history. A higher prevalence of DVT has been observed in hospitalized patients with COVID-19; CURB-65 score for pneumonia severity and raised D-dimer were significantly associated with DVT. COVID-19 positive patients with DVT had worse prognosis than those without, and patients with lower leg edema deserve further evaluation by using PoCUS for the lower legs and heart. COVID-19 carries a high risk of cardiac injury. In COVID-19 patients with arrhythmia, PoCCUS used by experienced hands may reveal abnormal RV functional parameters and lead to a more comprehensive cardiac US study. When there is suspicion of cardiac disease, PoCCUS can be done first, and if information is inadequate, limited conventional TTE and CCE can be followed. PoCCUS plays an important role in guiding the management of the cardiovascular disorders that

may accompany COVID-19. Cautious use of cardiac US can minimize exposure risk of the sonographers, operators, and patients. Proper and judicious application of PoCCUS may avoid the risk of contagion.^[40]

Preventing transmission of infection requires all health-care practitioners to implement both standard and transmission-based precautions, regardless of suspected or confirmed COVID-19. US practitioners should follow the standard precautions for COVID-19 as outlined by the Centers for Disease Control and Prevention. The PoCCUS performer should follow the institutional protocols. Workflow strategies should allow rest and recovery times during a shift, and all who perform ultrasound examinations should implement ergonomically correct scan techniques. Practitioners are also encouraged to use workflow strategies that minimize personal protective equipment turnover.^[2,41-44]

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