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# Echocardiography in COVID-19 Pandemic

## Clinical Findings and the Importance of Emerging Technology



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### KEYWORDS

• COVID-19 • Echocardiography • Myocardial strain • Ultramobile devices

### ECHOCARDIOGRAPHY IN COVID-19 PATIENTS

Coronavirus disease 2019 (COVID-19) mainly affects the respiratory system,<sup>1</sup> but important amount of evidence has described cardiac involvement,<sup>2,3</sup> in up to 20% of patients,<sup>4</sup> besides collaterally leading toward a change in hospital admission patterns for other cardiac diseases.<sup>5–7</sup> Echocardiography, as a widely available, cost-effective tool for the evaluation of cardiac structure and function, can provide important information that can affect the management of COVID-19 patients, but considering the risk of equipment contamination and personnel exposure,<sup>8</sup> focused evaluations instead of complete echocardiograms and the use of portable devices easy to disinfect, are recommended.

The present review discusses the principal echocardiographic findings in COVID-19 patients (Fig. 1; Table 1), practical aspects, and the role of emerging technology.

### LEFT AND RIGHT VENTRICLE: MAJOR FINDINGS

COVID-19 can cause a wide range of cardiac conditions, which include acute myocardial infarction,<sup>9–11</sup> takotsubo cardiomyopathy,<sup>12</sup> myocarditis,<sup>13</sup> arrhythmogenic,<sup>14</sup> thrombotic manifestations,<sup>15</sup> and potential drug-related effects,<sup>16–18</sup> as documented by several studies and early case reports.

However, the incidence of the cardiac involvement and the subsequent implications for treatment and resource allocation for the screening of these conditions are not well defined, but data confirmed that cardiac injury is associated with increased mortality in COVID-19.<sup>19,20</sup>

Regarding myocardial infarction, Stefanini and colleagues collected, in a national registry, 28 COVID-19 patients with ST-elevation myocardial infarction (STEMI): in approximately 40% of them, a culprit lesion was not detected by coronary angiography, pointing out the role of cytokine storm, hypoxic injury, coronary spasm, microthrombi, direct endothelial, or vascular injury. On echocardiography, about 80% of patients had localized left ventricular (LV) wall motion abnormalities, whereas left ventricular ejection fraction (LVEF) was less than 50% in about 60% of patients.<sup>21</sup>

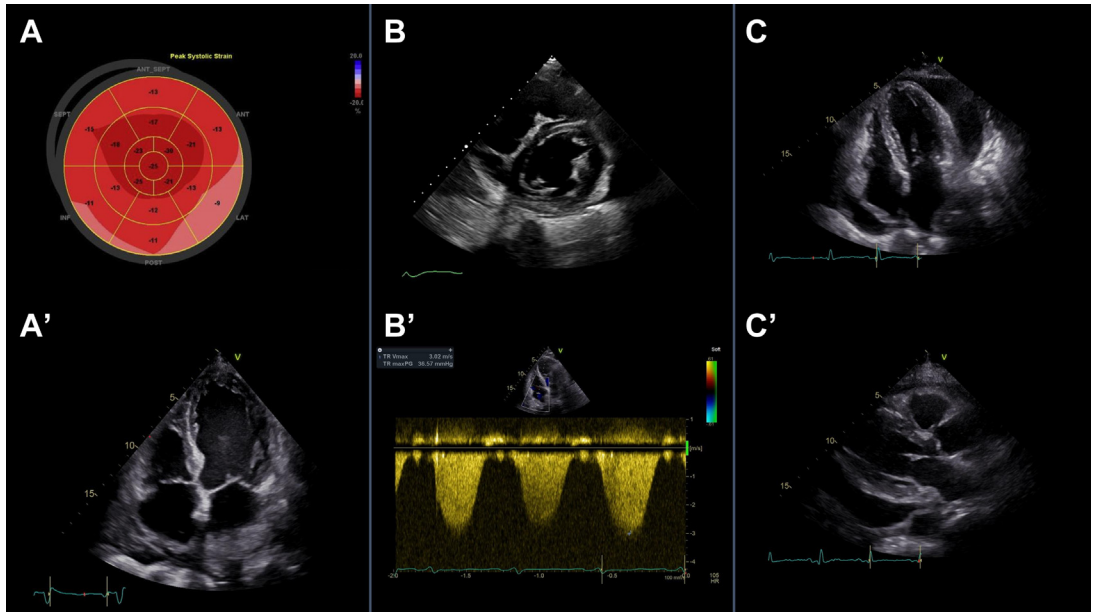
In COVID-19 have also been described cases of typical and atypical Takotsubo syndrome,<sup>22</sup> possibly triggered by emotional stress and physical stress by infection itself, with a significant increase in the incidence of stress cardiomyopathy when compared with prepandemic periods<sup>23</sup>: echocardiography has a diagnostic role in detecting the typical apical ballooning and possible unfavorable findings (LV outflow tract obstruction, mitral regurgitation, apical thrombus).<sup>24</sup>

Of particular interest, is COVID-19-related myocarditis: a direct cardiotropic localization of

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**Fig. 1.** Example of echocardiographic findings in different clinical settings of myocardial involvement in COVID-19 patients. Panel A and A': Reduced regional myocardial strain in lateral wall and dilation of left ventricle in myocarditis; Panel B and B': D-shape of left ventricle and increase in tricuspid regurgitation jet velocity in pulmonary embolism; Panel C and C': pericardial effusion, in parasternal long-axis and four-chamber view.

SARS-CoV-2 into myocytes has never been described, but some autoptic findings (lymphocyte infiltrates and macrophagic response) resulted compatible with viral myocarditis.<sup>25</sup> In a systematic review of Sawalha and colleagues

comprising 14 cases with myocarditis/myopericarditis believed to have occurred secondary to COVID-19 infection, echocardiography was performed in most cases (83%) and 60% had reduced LVEF, with diffuse hypokinesia in 30% of patients.<sup>26</sup>

However, excluding specific clinical scenario, while big alterations at conventional echocardiography could be difficult to detect,<sup>27</sup> deformation imaging can be the appropriate tool to identify subclinical modifications<sup>28</sup>: in a study of Stobe and colleagues, despite normal LVEF, most of the infected patients (that ranged from mild to severe symptoms) showed abnormal LV deformation, in particular a reduced longitudinal strain observed predominantly in more than one basal LV segment (in 10/14 patients, 71%), that was attributed to a possible subepimyocardial involvement of SARS-CoV-2-induced myocarditis, confirmed by cardiac magnetic resonance (CMR) but only in 2 patients.<sup>29</sup> Left ventricular-global longitudinal strain (LV-GLS) was altered in up to 80% of patients hospitalized for COVID-19 infection<sup>30</sup> (32/40 patients, mean LV-GLS of  $12.1\% \pm 4.0$ , normal  $<16\%$ ) and was superior to LVEF for predicting adverse outcome.<sup>31</sup> Indeed, an important role of echocardiography could be the prognostic stratification of patients: LV-GLS was found to be an independent predictor of mortality through multivariate analysis.<sup>32–34</sup>

**Table 1**  
Characteristics echocardiographic findings in different clinical settings of myocardial involvement in COVID-19 patients

Myocarditis	<ul style="list-style-type: none"> <li>• LV dilation</li> <li>• LV pseudohypertrophy</li> <li>• LV diffuse hypokinesia</li> <li>• Reduction in LVEF</li> </ul>
Acute coronary syndromes	<ul style="list-style-type: none"> <li>• Regional LV wall-motion abnormalities</li> <li>• Mechanical complications</li> </ul>
Pulmonary embolism	<ul style="list-style-type: none"> <li>• RV dilation with D-shape of LV</li> <li>• RV dysfunction</li> <li>• McConnell's sign</li> <li>• Increase in sPAP</li> </ul>
Pericarditis	<ul style="list-style-type: none"> <li>• Pericardial effusion, possible cardiac tamponade</li> <li>• Brightness of pericardium</li> </ul>

**Abbreviations:** LV, left ventricle; LVEF, left ventricular ejection fraction; RV, right ventricle; sPAP, systolic pulmonary arterial pressure.

A major role in COVID-19 is played by the right ventricle (RV): it could be affected secondarily to elevation in RV afterload; increases in PVR causes RV dilation and eventual RV failure, which has been related to a worse prognosis.<sup>35</sup>

COVID-19 could cause acute respiratory distress syndrome (ARDS) through vasoactive mediators, vascular thrombosis, and vascular compression secondary to atelectasis and edema.<sup>36</sup>

Moreover, patients with COVID-19 are in a prothrombotic state that predisposes them to thromboembolic events, including deep vein thrombosis and pulmonary embolism (PE).<sup>37–39</sup>

The study by Dweck and colleagues, a survey of the European Association of Cardiovascular Imaging, found that 33% of patients had an abnormal RV on echocardiography.<sup>40</sup> Of these subjects, 19% had mild-to-moderate RV dysfunction and 6% had severe dysfunction (of note, the index used for the definition of dysfunction was not specified). The RV was dilated in 15%, a D-shaped LV was seen in 4% and pulmonary artery pressure was elevated in 8%.

In the study by Mahmoud-Elsayed and colleagues, 41% of patients had a dilated RV (RV basal diameter >41 mm) and 27% had a decreased RV function (fractional area change <35% or a tricuspid annular plane systolic excursion <17 mm); most patients had severe respiratory failure and 82% were on invasive mechanical ventilation. A PE was detected in 20% of subjects with RV dysfunction as compared with 2% in those without RV dysfunction.<sup>41</sup>

Jain and colleagues found that 15.3% of the patients had an increased RV size (12.5% were mildly increased and 2.8% were moderately increased).<sup>42</sup> RV systolic function (assessed semi-quantitatively) was mildly decreased in 26.4%, moderately decreased in 9.7%, and severely decreased in 4.2%.

Several studies reported an association between right-side TTE parameters and prognosis in patients with COVID-19.

Kim and colleagues in an analysis from a US multicentre retrospective study reported that adverse RV remodeling (dysfunction/dilation) conferred a >2 fold increase in mortality risk.<sup>43</sup>

Szekely and colleagues<sup>44</sup> found that the most frequent abnormality among patients with clinical deterioration during follow-up was RV dilatation (with or without dysfunction). In univariable analysis, they reported that shorter pulmonary acceleration time (<100 msec) was associated with clinical deterioration and that RV end-diastolic area was associated with mortality.<sup>44</sup>

Li and colleagues reported that RV global longitudinal strain was a powerful predictor of death in patients with COVID-19.<sup>45</sup>

In a recent systematic review, Messina and colleagues analyzed studies available in literature and concluded that they have highly variable sample sizes and reported highly heterogeneous findings: LVEF does not seem significantly affected (reported as higher than 50% in most subjects), LV diastolic function has not been properly assessed and RV dysfunction seems frequent but defined with variable criteria, making it difficult to establish a clear association with higher mortality.<sup>46</sup>

## CARDIAC VALVES AND PERICARDIUM

The presence of valvular heart disease (VHD) has been described in COVID-19 patients undergoing echocardiography during the hospital stay.<sup>40</sup> These valvular diseases more likely were present before the onset of SARS-CoV-2 infection. A recent study regarding echocardiographic findings among COVID patients reported that half of them presented a significant tricuspid regurgitation followed by aortic regurgitation and mitral regurgitation.<sup>47</sup> Tricuspid regurgitation is the most common VHD reported in COVID-19 patients and its severity could directly reflect the impairment of the pulmonary circulation during the infection resulting in pulmonary hypertension, especially in patients with severe pneumonia and respiratory insufficiency.<sup>48</sup>

A higher concern, especially in COVID-19 patients in the intensive care unit, is the presence of infectious endocarditis (IE). Some clinical reports have reported endocarditis in a minority prevalence and the presence of valve vegetations were also described in autopsy findings for SARS-CoV-2 patients.<sup>40,49</sup> In this setting, endocarditis is related to bacterial endocarditis or the presence of thrombus; less likely could be caused by the direct SARS-CoV-2 infection and there is no evidence about that relationship.

According to the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) recommendations, in case of suspected or confirmed SARS-CoV-2 infections, cardiac imaging should be considered only on an individual basis when it could change the clinical management or be life-saving for the patients, because of the higher risk of contamination for health care providers, especially during transesophageal echocardiography (TOE).<sup>50,51</sup> Despite that, TOE remains the gold standard for the diagnosis of IE even in the current COVID-19 pandemic and to better evaluate the severity of a significant VHD.<sup>52,53</sup> In conclusion,

in COVID-19 patients with high suspicion of IE or significant VHD, explorative TTE and if inconclusive a subsequent TOE is mandatory for the diagnosis with all the precautions aimed at avoiding the spread of the infectious disease.

Some case reports reported acute pericarditis during SARS-COV-2 infection.<sup>54</sup> This type of cardiac involvement is often seen in patients with troponin elevation in the context of myocardial damage and less frequently as a primary presentation of COVID-19 infection, which occurred most in younger patients.<sup>55,56</sup> Pericardial involvement may be driven by the systemic and local inflammatory response to infection and less likely by direct virus damage.<sup>57</sup> Another form of pericardial involvement is pericardial effusion, found in nearly 5% of COVID-19 patients who underwent chest CT.

As recommended by ESC guidelines, also in patients with SARS-CoV-2 infection, TTE is recommended as the first diagnostic tool to evaluate pericardial diseases and it is most useful to address the severity of significant effusion.<sup>58</sup> As second step, in selected cases because of logistic issues in this setting, CMR can evaluate pericardial thickening or small effusions, assess myocardial damage, and precisely define pericardial inflammation.<sup>59</sup>

## PRACTICAL ASPECTS

Since the beginning of the pandemic, concerns have been raised about the risk of performing echocardiograms for the risk of personnel infection, with the subsequent need to select patients in which echocardiography can have a fundamental diagnostic/prognostic role. The principal echocardiography societies released recommendations to review the appropriateness of every examination, favor the use of handheld devices (easier to disinfect) and perform fast and focused evaluations: they provided a modified point-of-care ultrasound (POCUS) protocol for the evaluation of patients with suspected or confirmed COVID-19, when is likely to have an impact on patient management (summary recommendations in **Box 1**).<sup>50,60</sup> Adopting protocols aimed at reducing the number of inappropriate studies, the workflow in echocardiography laboratories has declined by 50% and the study appropriateness has significantly increased.<sup>61</sup> Moreover, the use of limited tablet-based echocardiograms can reduce the study time by 79%.<sup>62</sup> Considering the importance of prone position in patients developing ARDS, some reports have suggested that prone position echocardiography might be feasible, allowing RV and LV evaluation in a four-chamber view.<sup>63</sup>

### Box 1

#### Summary recommendations for echocardiography in COVID-19 patients

##### Indications

- Perform urgent/emergent examinations (that can change patient management or be life-saving, in particular for TOE)
- Defer elective/routine follow-up examinations

##### Personnel protection

- Droplet precautions for TTE (protective clothing, gloves, headcovers, specific face-masks, and eye shields)
- Airborne precautions for TOE (N-95 or N-99 respirator masks)
- Patients should wear a surgical mask during imaging

##### Method

- Focus cardiac ultrasound study:
  - LV: LVEF, regional dysfunction, end-diastolic cavity dimension
  - RV: TAPSE, end-diastolic cavity dimension, tricuspid regurgitation pressure gradient
  - Valves: gross signs of valvular disease
  - Pericardium: thickening or effusion
- ECG monitoring can be omitted

##### Technology

- Prefer hand-held or smaller lap-top-based scanners
- Measurements should be performed offline

*Abbreviations:* LV, left ventricle; LVEF, left ventricular ejection fraction; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; TOE, transesophageal echocardiography; TTE, transthoracic echocardiography.

## DEVELOPMENT OF NEW TECHNOLOGIES

The need for absolute isolation of symptomatic patients and the high possibility of spreading the infection outside the isolation rooms in the high-intensity care departments, makes any attempt at an instrumental diagnostic approach difficult, given also the absolute need to decontaminate the equipment used after each individual examination. The advantages deriving from the execution of echocardiography examination at the patient's bedside are well known but the high risk of serious coronavirus infection diffusion has made its use difficult. Disinfection is the only way to counter the risk of spreading the disease from one patient to another

or among the operators themselves, which event is even more dangerous because it would jeopardize the tightness of the system. Hand-carried echocardiography devices offer rapid and readily available information at the bedside, as they help overcome the problems caused by the use of cumbersome standard equipment.<sup>62,64</sup> The use of “ultramobile devices” has recently been introduced in the area of cardiovascular ultrasound diagnostics. These devices are miniaturized systems equipped with diagnostic quality two-dimensional (2D) and color Doppler imaging. With simplified criteria, they can detect LV dysfunction and moderate-severe valvulopathy with good sensitivity and specificity. They are extremely useful in the immediate diagnosis of pericardial effusion and in the definition of states of cardiocirculatory failure or inflammatory states of pulmonary parenchyma. In resource-limited settings, ultramobile systems can reduce the need for standard echocardiography. “Ultramobile” systems have a probe that can be connected to any handheld device, smartphone, or tablet, allowing the execution of cardiac, pulmonary, vascular, abdominal, soft tissue, and joint ultrasound. The isolation system, required to avoid the danger of spreading the infection, is simple, consisting of a mono-use coating sheath commonly used for epicardial echocardiography in the cardiac surgery operating room. At the end of the examination, the probe is removed from the casing, reinserted in a new protective sheath, and ready for a subsequent examination. The compactness of the system makes it easily isolable from the environment with a mono-use coating sheath, making it very practical in environments with a high level of contamination or where absolute sterility is required. Thanks to Internet connectivity, the images, stored in DICOM format, can also be simultaneously viewed in real time by other doctors outside the contaminated area: data collection and their quick transfer allow a postprocedural analysis in the safe zone. Finally, a video call system allows communication between operators. Moreover, this aspect gives the possibility to exploit few medical imaging experts for the interpretation of examinations from numerous Spot Centers, also performed by doctors or trained nonmedical staff not specialized in imaging.

Moreover, in China, a pilot study of robot-assisted teleultrasound based on 5G Network was conducted<sup>65</sup>: ultrasound specialists carried out the robot-assisted teleultrasound, manipulating a handheld controller, which can control the robotic arm, and did remote consultation in order to settle the problem of early cardiopulmonary evaluation in COVID-19 patients.

A point of particular importance is the role of artificial intelligence (AI), technology that creates

a computerized model to solve different problems without the requirement of human assistance, continuously learns from the data set, and predicts outcomes accurately.<sup>66,67</sup> It was used in intensive care unit by critical care physicians without formal training in ultrasound to obtain POCUS images, with the use of real-time prescriptive guidance to direct the physician’s transducer position and hand movements to acquire the images, automatically capturing them when appropriate, detecting LVEF with high accuracy, and uploading to the archive and communication system for offline review.<sup>68</sup> AI includes machine learning (ML), which offers the potential to improve the accuracy and reliability of echocardiography by combining clinician interpretation with information derived from ML algorithms. In conclusion, high volume data generated from cardiac imaging can be integrated into a multiparametric approach for pattern recognition and imaging data-based disease phenotype characterization, particularly useful and time-saving in the setting on COVID-19 pandemic.<sup>69</sup>

## SUMMARY

Echocardiography has a diagnostic and prognostic role in COVID-19, helping in recognizing cardiac involvement. Considering the high risk of personnel infection and equipment contamination, focused echocardiographic protocols with portable devices are recommended.

Available echocardiographic data on COVID-19 patients actually do not provide definite evidence, due to multiple factors: high heterogeneity between studies in numbers of patients, miscellaneous results, and low quality of echocardiographic studies for technical difficulties in performing bedside procedures (patients with respiratory distress/invasive ventilation; while wearing personal protective equipment).

In conclusion, echocardiography represents an important tool in the management of COVID-19 patients, but more studies with standardized acquisitions and methods are needed to describe definite echocardiographic findings in this setting.

## CLINIC CARE POINTS

- Focused echocardiographic protocols can detect cardiac involvement in COVID-19
- Echocardiography is strictly recommended if it could change the clinical management

- Available data do not provide definite evidence on echocardiographic findings in COVID-19

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