The role of echocardiography in SARS-CoV-2 pandemic: a compromise among appropriateness, safety and clinical impact

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Abstract

SARS-CoV-2 infection, responsible for COVID-19, can determine cardiac events, which require a quick diagnosis and management, and should not be overlooked due to the presence of COVID-19 infection. In some cases, cardiovascular symptoms can also be the first and only manifestation of SARS-CoV-2 infection. In patients with COVID-19, the full cardiovascular disease diagnostic algorithm can be hindered by logistic restrain mainly derived from the difficulty of transporting patients in critical conditions to Radiology or Hemodynamics wards. The echocardiography in SARS-CoV-2 pandemic can help for differential diagnosis of cardiac events, which can be related or unrelated by the infection and can likely impact on short-term prognosis. Indeed, transthoracic echocardiography plays a key role in the screen for CV complications of COVID-19 infection: it must be focused cardiac ultrasound study (FoCUS) performed at bedside. All transthoracic, transesophageal and stress echocardiograms in patients in which test results are unlikely to change the management strategy should be postponed.

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In these weeks of great national emergency we have learned that SARS-CoV-2, the virus responsible for COVID-19, can determine cardiac events, which can be related to the infection including acute coronary syndromes (STEMI and NSTEMI), acute heart failure, arrhythmias, myocarditis, pericarditis, thromboembolic events, cardiogenic shock, and cardiac arrest. Those syndromes require a quick diagnosis and management, and should not be overlooked due to the presence of COVID-19.

Cough, fever, tiredness and difficulty breathing compose the "classic" COVID-19 symptoms; some SARS-CoV-2 positive patients have anosmia and dysgeusia and gastrointestinal disturbances. Moreover, these patients often show symptoms mimicking cardiovascular events, including chest pain, dyspnea, and shock, even in the absence of cardiac injury. In some cases, cardiovascular symptoms can also be the first and only manifestation of SARS-CoV-2 infection [1,2].

Some positive patients are admitted to the emergency room with palpitations and tachycardia, chest tightness or pain, and drop attack or syncope. These disorders are caused by arrhythmias, acute myocardial infarction, acute heart failure, myocarditis and pericarditis. Indeed, associated profound hypoxemia related underlying pneumonia together with tachycardia might result in chest pain and electrocardiographic changes suggestive of myocardial ischemia. The prevalence of cardiac injury is estimated up to 20% of cases. The severity of cardiac involvement is closely related to the severity of clinical scenario and mortality in these patients [3-7].

The appearance of acute myocardial injury is not early but it usually occurs at least 10 days after the appearance of fever [5,8]. Cardiomyocyte injury, as quantified by cardiac troponin T/I concentrations, and hemodynamic stress, as quantified by B-type natriuretic peptide (BNP) and N-terminal B type natriuretic peptide (NT-proBNP) concentrations, may occur in as in COVID-19 infections as in other pneumonias. The level of those biomarkers

correlated with disease severity and mortality [5,6]. Concentrations of these biomarkers remained within the normal range in the majority of survivors; however, in non-survivors, troponin levels progressively increased in parallel with the severity of COVID-19 and ARDS development [6,9,10].

During the acute phase, the occurrence of overall reduction of systolic function of the left ventricle can be assessed by echocardiography, in the absence of previous history of systolic dysfunction cardiomyopathy, especially in patients with clinical signs of cardiogenic shock admitted to Intensive Care Unit [11].These features are usually seen in other conditions characterized by cytokine-mediated responses such as septic shock, where the release of cytokines can determine reduction of the ejection fraction and increase in the volume of the chambers ventricles [12]; and in acute myocardial infarction, where the cytokine response contributes to the mechanisms of cardiogenic shock [13]. Therefore, studies aiming at clarifying the peculiarity of this type of cardiac impairment during COVID-19 are eagerly encouraged.

Myocarditis and pericarditis are other manifestations of cardiac involvement from SARS-CoV-2 occurring sometimes before the onset of pulmonary symptoms shock [14-16]. In addition, myocardial injury with ST-segment elevation on electrocardiography has been observed in patients with Covid-19. These patients have variability in presentation, a high prevalence of non-obstructive disease, and a poor prognosis shock [16-18]. It has been reported the presence of SARS-CoV-2 in the pericardial fluid of a patient with COVID19 and cardiac tamponade subjected to pericardiocentesis shock [19].

The mechanism underlying acute myocardial injury is not fully elucidated; however, a direct cardiac injury could be hypothesized. In some cases, the SARS-CoV-2 can cause direct damage to myocytes mediated by stimulation of the angiotensin-converting enzyme 2 (ACE2), which is expressed on myocytes and vascular endothelial cells, acting as a receptor for SARS-CoV-2 and as "gateway" for the virus in these cells. Another hypothesized mechanism is myocardial damage induced by hypoxia and activation of the innate immune response with release of pro-inflammatory cytokines: a real inflammatory storm, as well as to the activation of adaptive auto-immune which can induce vascular and myocardial inflammation and an excess of blood clotting, which cause episodes of diffuse thrombosis shock [9].

In patients with COVID-19, the full cardiovascular disease diagnostic algorithm can be hindered by logistic restrain mainly derived from the difficulty of transporting patients in critical conditions to Radiology or Haemodynamics wards. Therefore, Transthoracic (TT) Echocardiography shock [18] plays a key role in the initial diagnostic phase, since it can be performed bedside. However, it should be considered that in COVID-19 patients, echocardiography should be carried out according to the guidance provided by scientific societies shock [19], limiting the exposure time of the operators at the acquisition of images strictly necessaries (Table 1). Focused cardiac ultrasound study (FoCUS) performed at bedside is an effective option to screen for CV complications of COVID-19 infection. It should not be forgotten that the risk of infection remains in the reading rooms and therefore the device should be also frequently sanitized. Finally, the quality of echocardiography can be compromised in intubated patients shock (Figure 1) [18-22].

Non-urgent or elective cardiac imaging should not be performed routinely in patients with suspected or confirmed COVID-19 infection and should be postponed until the infection has terminated [21]. All transthoracic, transesophageal and stress echocardiograms in patients in which test results are unlikely to change the management strategy should be postponed.

In this clinical scenario, echocardiography is useful for evaluating regional or global anomalies of the contractility of the left ventricle, and documenting the possible acute overload of the right ventricle, in case of ARDS or pulmonary embolism, especially in presence of hemodynamic instability [20].

A single ultrasound system should be identified, preferably portable and with reduced dimensions to facilitate sanitation; probe covers should be used, and a single operator with sufficient experience (not in training) should perform the examination. The final exam scan should be a good compromise between adequacy and speed of execution (limited ultrasound sections, bimodal responses with high clinical impact, image registration and subsequent "off line" review).

Table 1. Schematic representation of echocardiographic parameters for the assessment of COVID-19 patients and suspected cardiovascular involvement.

Cardiac chamber	Clinical question	What to analyze
Left ventricle	Septic shock Significant troponin increase Suspected myocarditis	Increased LV size (diameters or volumes) Reduced LV ejection fraction Impaired LV Segmental contractile function LV diastolic dysfunction (E/e')
Left atrium	Supraventricular arrhythmias	Increased LA size (diameter or volume)
Right ventricle	Pulmonary embolismInvasive or noninvasive ventilation with unstable hemodynamics	Increased RV size (diameters) Dilated RV with basal RV/LV ratio >1.0, and McConnell sign Decreased tricuspid annular plane systolic excursion (TAPSE) Pulmonary hypertension (increased PASP)
Inferior vena cava	Hemodynamic impairment	Distended IVC with reduced inspiratory collapsibility
Pericardium	Pericarditis Suspected cardiac tamponade	Pericardial effusion Right heart chamber collapse Doppler signs of tamponade

LV, left ventricle; RV, right ventricle; PASP, pulmonary artery systolic pressure; IVC, inferior vena cava.

Particular attention should be paid to the execution of transesophageal echocardiogram (TEE). TEE carries increased risks of spread of COVID-19 due to exposure to aerosol of large viral load and it should not be performed if an alternative imaging modality is available. TEE must be carried out with complete personal protective equipment (*i.e.*, mask at least N95 according to American classification or FFP2 according to the European classification).

To date, studies focused on Doppler-echocardiography parameters conducted specifically in cohorts of COVID-19 patients are lacking. However, the role of echocardiography in monitoring biventricular function during sepsis and septic shock is well known. Most studies on acute myocardial dysfunction during sepsis have been conducted in patients admitted to intensive care and subjected to mechanical ventilation, using TT and TEE echocardiography [24,25]. These studies show that about 30-40% of septic patients develop reduction of the ejection fraction of the left ventricle, impaired diastolic function of the left ventricle and possible impairment of the function of the right sections in particular during ARDS [26,27].

Another aspect that should be underlined is the hemodynamic effect of ventilation on cardiac performance [29,29]. Positive end-expiratory pressure (PEEP), increasing lung size, can cause an increase in pulmonary vascular resistance (RVP), due to the compression of alveolar and extra-alveolar capillaries; as a consequence, there is increase in post-load and right ventricle volume (VD), shift of the interventricular septum to the left and reduction of compliance and filling of the left ventricle. However, since the increase in RVP is countered by the elimination of hypoxia-induced vasoconstriction, increase in RVP becomes relevant only for high PEEP values. In addition, the increase in intrathoracic pressure determines a subsequential increase in intrathoracic veins resistance, that represents a mechanism reducing the gradient and venous return for VD, especially in conditions of true (anemia, dehydration, *etc*., in a healthy heart) or relative (severe right ventricular dysfunction) hypovolemia. This phenomenon, however, is counterbalanced by the increase in abdominal pressure due to the diaphragm lowering with the effect of live and spleen "squeezing". Therefore, in clinical practice, the potential negative hemodynamic effects of PEEP (hypotension secondary to reduced preload and increased VD afterload) are mainly confined to patients highly dependent on preload, and can be partially balanced by carrying out a preventive volemic filling (Figure 2) [29-31].

Therefore, in this particular period, we have to be careful to possible cardiological symptoms of COVID-19. The echocardiography in SARS-CoV-2 pandemic can help for differential diagnosis of cardiac events, that can be related or unrelated by the infection but can be determinants for the short-term prognosis.

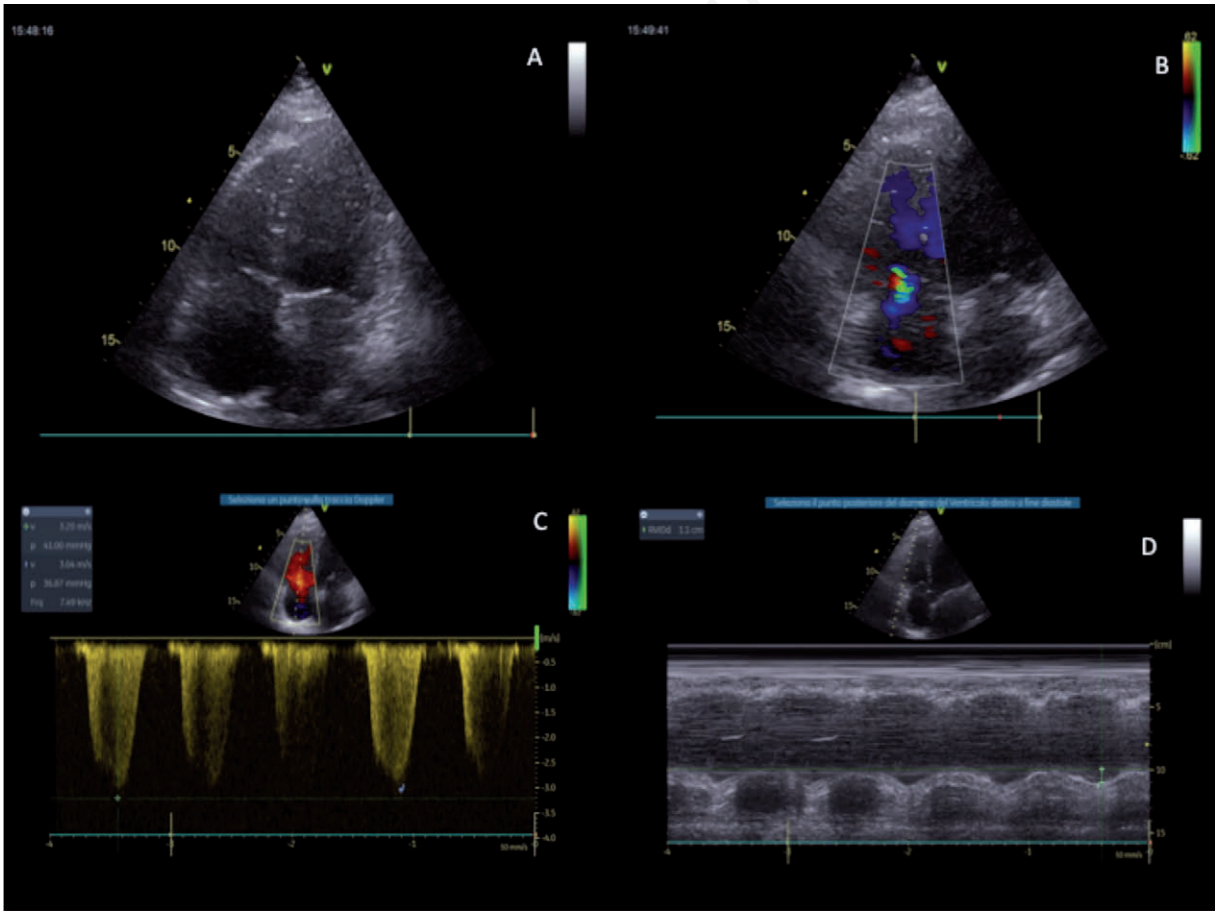

Figure 1. 65-year-old male patient, affected by COVID pneumonia, intubated, increased levels of troponin and D-Dimers, and negative CUS. Normal size of the left ventricle and normal ejection fraction, mild dilation of the right ventricle (A), mild tricuspid regurgitation (B), increased PAPs (C) and severe contractile dysfunction of the right ventricle, with reduced tricuspid annular plane systolic excursion (TAPSE) (D).

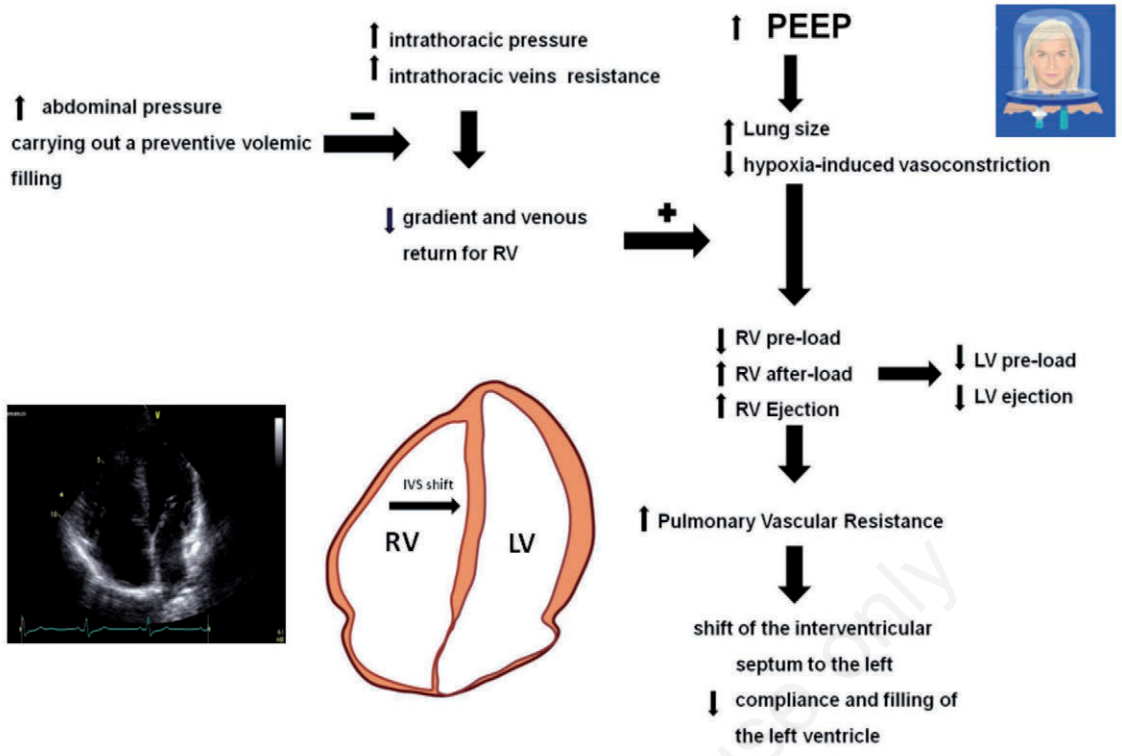

Figure 2. Hemodynamic effects of ventilation on cardiac performance. PEEP, positive end-expiratory pressure; RV, right ventricle. LV, left ventricle; IVS, interventricular septum.

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