

# Echocardiographic patterns in critically ill COVID-19 patients.

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## Research

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# Abstract

**Background:** Need for catecholamines is frequent in COVID-19 patients, but the main echocardiographic patterns are unknown. The objective was to report the main echo patterns in critically-ill COVID-19 patients.

**Methods:** Observational and descriptive study in consecutive COVID-19 patients admitted to the ICU between March 12 and May 8, 2020. Systematic critical care echocardiography (CCE) was performed and retrospectively analyzed off-line. Echo values are reported in the overall population and in patients who required catecholamine infusion during the first 2 days following admission ( $D_{1-2}$ ) or afterwards until day 7 ( $D_{3-7}$ ).

**Results:** Of the 79 patients (78% male; median age 63 [56-71]; body mass index 29 [26-30]) included, 90% had at least 1 comorbidity.  $PaO_2/FiO_2$  at admission was 85 [67-162] mmHg. 53% of patients were mechanically ventilated. ICU length of stay was 9 [5-16] days and mortality 34%. 134 echocardiographic studies were performed during the first week in 65 patients. Pulmonary artery acceleration time was decreased (77 [65-97] ms), suggesting pulmonary hypertension. All 39 patients (49%) who required catecholamine infusion underwent CCE and 25.6% had left ventricular (LV) systolic dysfunction, 28.2% acute cor pulmonale (ACP), 7.7% hypovolemia, and 38.5% vasoplegia. Modification of echo patterns was observed at  $D_{3-7}$ , with less LV systolic dysfunction and more ACP, which was the most frequent pattern. Computed tomography pulmonary angiography in 6 patients with ACP indicated intrapulmonary thrombus in 4.

**Conclusion:** Different echocardiographic patterns were observed during the first week following ICU admission in COVID-19 patients. ACP was frequent and often related to thrombus in the pulmonary circulation.

## Background

Bhatraju et al. recently reported that 71% of 24 critically ill COVID-19 patients required vasopressor infusion more than 12 hours after intubation [1]. Many studies have reported that myocardial injury and heart failure are frequent in COVID-19 patients and are common causes of death [2, 3]. Spectrum of the COVID-19 cardiovascular syndrome is large with different potential mechanisms supporting acute myocardial injury [4]. COVID-19 frequently induces pulmonary artery thrombosis [5]. The cytokine storm may also induce vasoplegia and distributive shock and COVID-19-related pneumonia may lead to acute respiratory distress syndrome (ARDS) [6], a condition well known to alter right ventricular (RV) function [7]. As a consequence, many different mechanisms may explain the circulatory failure frequently observed in COVID-19 patients.

However, to the best of our knowledge, there is currently no information about cardiac function and echocardiographic patterns in COVID-19 patients. Most studies only report a few echocardiographic

studies or biomarkers as troponin [3]. Data are urgently required to understand this new disease and to improve hemodynamic support in these patients. We have performed critical care echocardiography (CCE) in most patients admitted to our ICU for more than 25 years [8]. The objective of our study is to describe the main echocardiographic patterns during the first 7 days of patients admitted to our ICU for COVID-19.

## Material And Methods

In this retrospective, single-center, observational study in a university-affiliated hospital in Paris (AP-HP), we enrolled all consecutive patients with laboratory-confirmed SARS-CoV-2 infection admitted between March 12 and May 8, 2020. The ethics committee of the French Society of Intensive Care Medicine approved the study (CE-SRLF 20–40). We especially noted the sequential organ failure assessment (SOFA) score [9] at day 1, body mass index (BMI), medical history, duration of symptoms before ICU admission, serum lactate and PaO<sub>2</sub>/FiO<sub>2</sub> at admission. Computed tomography pulmonary angiography (CTPA), when performed, was also recorded and pulmonary embolism was considered in the case of positive CTPA or when thrombus was present in the right chambers on CCE, which has been a routine procedure in our unit for more than 25 years. ARDS was defined using the Berlin definition [10]. In-ICU mortality and length of ICU stay were recorded. Because we performed serial echo studies in patients during their ICU stay, we are able to report findings of the first CCE performed when patients required catecholamine infusion, differentiating 2 periods of time during the first week (D<sub>1-7</sub>), one during the first 2 days following admission (D<sub>1-2</sub>) and the second during the following days (D<sub>3-7</sub>). The main clinical and laboratory results were extracted from the electronic medical records.

## Procedure and parameters of critical care echocardiography studies

All studies were prospectively performed using a Vivid E9 or Vivid S70 ultrasound system (GE Healthcare, 78530 Buc, France) by the transthoracic (TTE) or transesophageal (TEE) route, the latter only in mechanically ventilated patients. Echo data were all recorded and reanalyzed off-line using the Echo-PAC software (GE Healthcare, 78530 Buc, France) by 2 investigators with academic expertise in the field (AVB, CC) and blinded to patient status. Briefly, on an apical four-chamber view (TTE) or a transverse mid-esophageal view (TEE), left ventricular ejection fraction (LVEF) was calculated by the Simpson method [11], and the size of the right ventricle was evaluated using the end-diastolic area ratio of the right to the left ventricle (RV/LV EDA) [12]. Any LV segmental wall abnormalities were noted. Pulsed Doppler of the mitral inflow allowed determination of the E/A ratio. Any paradoxical septal motion was noted on a parasternal short-axis view (TTE) or a transgastric view (TEE). The velocity time integral (VTI) in the left outflow tract was determined using pulsed-wave Doppler and was used as a surrogate for LV stroke volume. The pulmonary artery acceleration time in the RV outflow tract (PAAcT) was recorded using pulsed-wave Doppler and was used as a marker of pulmonary hypertension (normal value > 100 ms) [13]. Respiratory variation of the superior vena cava ( $\Delta$ SVC) was calculated on a longitudinal upper-

esophageal view. Finally, we noted any thrombus in the right chambers or in the pulmonary arteries (by TEE).

## Main definitions of echocardiographic patterns

LV systolic dysfunction was defined as an LVEF < 45%. Acute cor pulmonale (ACP) was defined as an RV/LV EDA > 0.6 associated with paradoxical septal motion [12]. Hypovolemia was defined by a  $\Delta$ SVC > 20% [14] frequently associated with a hyperkinetic left ventricle and end-systolic exclusion. Finally, vasoplegia was diagnosed in the absence of any of these abnormalities, a situation where LV systolic function was frequently in the normal or supranormal ranges [15].

## Statistical analysis

We only used descriptive statistics to report the main characteristics of the population and the echocardiographic findings. Values were reported as median [interquartile range] for quantitative variables and counts and percentages for qualitative variables.

## Results

The main characteristics at admission of the 79 consecutive patients included are reported in **Table 1**. 62 (78%) were male. Median age was 63 [56-71] years and BMI 29 [26-30]. Chronic medical conditions were present in 90% of patients, the main ones being hypertension (40%). Chronic heart failure was reported in 11% of patients. Median duration of symptoms before ICU admission was 8.5 [1-10] days. Seventy-seven patients were admitted for severe pneumonia requiring high oxygen flow and the 2 others for shock related to Kawasaki-like syndrome. Median temperature at admission was 39°C [38-39] and PaO<sub>2</sub>/FiO<sub>2</sub> 85 [67-162] mmHg. Median SOFA score at day 1 was 4 [3-5]. Forty-two (53%) patients were mechanically ventilated, 39 for ARDS, which was severe in 35 with a PaO<sub>2</sub>/FiO<sub>2</sub> < 100 mmHg. All non-ventilated patients required a high-flow oxygen nasal cannula, and all but 2 had a PaO<sub>2</sub>/FiO<sub>2</sub> < 300 mmHg, 20 of them with a PaO<sub>2</sub>/FiO<sub>2</sub> < 100 mmHg. Overall, 39 (49%) patients required catecholamine infusion during D<sub>1-7</sub>, 24 during D<sub>1-2</sub>, and 15 more during D<sub>3-7</sub>. Median length of stay was 9 [5-16] days and in-ICU mortality was 34.2% (all patients had been discharged from the ICU at the time of this analysis).

**Table 1:**

Main characteristics of the population at admission and outcome.

BMI: body mass index, COPD: chronic obstructive pulmonary disease

Age (years)	63 [56-71]
BMI	29 [26-30]
Gender (male, n, %)	62 (78%)
Medical history (%)	
Tobacco smoker	30%
COPD	5%
Asthma	5%
Hypertension	40%
Diabetes mellitus	33%
Chronic heart failure	11%
Immunodeficiency	8%
Chronic kidney disease	4%
Duration of symptoms before ICU admission (days)	8.5 [1-10]
Temperature (°C)	39 [38-39]
SOFA score day 1	4 [3-5]
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	85 [67-162]
Lactate (mmol/L)	1.18 [1-1.64]
In-ICU length of stay (days)	9 [5-16]
ICU mortality, n (%)	27 (34.2%)

One hundred thirty-four CCE were performed in 65 patients during D<sub>1-7</sub>, 70 TEE and 64 TTE. CCE was performed in all patients requiring catecholamine infusion. Systematic CCE was also performed in 26/40 patients without catecholamine infusion (**Figure 1**). Results of CCE in the population during D<sub>1-7</sub> are reported in **Table 2**. PAAcT was decreased, with a median of 77 [65-97] ms. In patients who required catecholamine infusion, LV systolic dysfunction was observed in 10 (25.6%), with a median LVEF of 28% [20-37]. LV end-diastolic volume was in the normal range (111 [80-118]) and VTI decreased (16 [11-16]). This pattern included 2 young women, respectively 17 and 24 years old, admitted for a Kawasaki-like syndrome (videos are given in **additional files 1-2**). ACP was observed in 11 (28.2%) patients with a median RV/LV EDA of 1.1 [0.9-1.3] and a PAAcT of 71 [55-88] ms. In 3 (3.8%) patients with ACP, thrombus was visualized by CCE in the right pulmonary artery or in the right atrium (videos are given for 2 cases in **additional files 3-4 and 5-7**). In this specific pattern, CTPA was performed in 6/11 patients (the others were too unstable to be mobilized) and found intrapulmonary thrombus in 4 (67%). Persistent hypovolemia was observed in 3 (7.7%) patients with a median  $\Delta$ SVC of 25% [23-38] (illustrations with videos are given in **additional files 8-9**). Vasoplegia was observed in 15 (38.5%) patients (illustrations with videos are given in **additional files 10-11**). Pericardial effusion was rare (7.7%), no cardiac tamponade was diagnosed and segmental wall motion abnormalities were observed in 18%. Echo patterns were different during the 2 periods (**Figure 2**). While vasoplegia remained constant, incidence of

ACP was much more pronounced during D<sub>3-7</sub> where ACP was the most frequent pattern. CCE was in the normal ranges in the 26 patients who did not require catecholamine infusion (median LVEF of 66% [56-74], RV/LVEDA of 0.56 [0.50-0.56] and VTI of 20 cm [18-23]).

**Table 2:**

Values of main parameters of echocardiography performed during D<sub>1-7</sub> for the overall population (n = 65), and for the 39 patients when catecholamine infusion started according to the echo patterns.

	Overall population (n = 65)	LV systolic dysfunction (n = 10 )	ACP (n = 11)	Hypovolemia (n = 3)	Vasoplegia (n = 15)
LVEF (%)	60 [49-70]	28 [20-37]	60 [50-64]	63 [61-69]	63 [60-67]
LVEDV (mL)	97 [82-120]	111 [80-118]	86 [40-91]	100 [91-109]	86 [78-107]
RV/LV EDA	0.55 [0.5-0.61]	0.51 [0.5-0.6]	1.1 [0.9-1.3]	0.57 [0.55-0.60]	0.53 [0.49-0.59]
ΔSVC %	8 [0-21]	5 [0-11]	1 [0-7]	25 [23-38]	2 [0-6]
Aortic VTI (cm)	17 [15-21]	16 [11-16]	15 [14-20]	17 [14-20]	19 [17-22]
E/A ratio	0.93 [0.7-1.2]	1.27 [0.99-1.84]	0.91 [0.6-1.1]	0.67 [0.61-0.72]	0.91 [0.7-0.97]
PAAcT (ms)	77 [65-97]	62 [52-86]	71 [55-88]	66 [59-84]	87 [77-95]

LVEF: left ventricular ejection fraction, LVEDV: left ventricular end-diastolic volume, RV/LV EDA: right ventricular/left ventricular end-diastolic area, ΔSVC: respiratory variation of the superior vena cava, VTI: velocity time integral, PAAcT: acceleration time of the right ventricular ejection flow.

## Discussion

To the best of our knowledge, we report here the first case series of echocardiographic patterns in critically ill patients admitted for COVID-19. This study was enabled by our systematic and protocolized use of CCE for more than 25 years. Among the 79 patients admitted during the study period, 65 underwent CCE during the first week, in 39 cases because they required catecholamine infusion and in 26 cases systematically. The most frequent echo pattern was vasoplegia ( $\approx$  38%), followed by ACP ( $\approx$  28%), LV systolic dysfunction ( $\approx$  25%), and hypovolemia ( $\approx$  8%). Changes in echo patterns were observed when CCE was performed during D<sub>3-7</sub>, with more patients exhibiting ACP. Interestingly, all patients had a decrease in pulmonary acceleration time (PAAcT).

The pattern of ACP is probably the one which deserves the most discussion. It was the most frequent pattern during D<sub>3-7</sub>. We found thrombus in the pulmonary arteries in 67% of cases when CTPA was

performed. Significant coagulopathy with clinical consequences has been reported in COVID-19 [16]. In an autopsy series of 12 patients, Wichmann et al. reported a high incidence of deep venous thrombosis and pulmonary embolism [5]. In 337 COVID-19 patients who underwent CTPA, Poyiadji et al. reported pulmonary embolism in 22% of cases [17]. Another explanation for ACP is distal microthrombosis of the pulmonary circulation due to extensive inflammation in the lung. This was noted in 7 lungs from patients who died from COVID-19 by Ackermann et al., who especially reported alveolar capillary microthrombi and severe endothelial injury [18]. The fact that our patients had a decrease in pulmonary artery acceleration time, even without ACP, suggests that most of them had a certain degree of pulmonary vascular dysfunction with pulmonary hypertension. In more “usual” ARDS, RV failure has also been suspected to be related to respiratory settings and alveolar overdistension. It is unlikely that such a mechanism could act in this specific situation as COVID-19 patients have near-normal lung compliance and are easily ventilated, at least during the first days [6] but larger studies are needed.

The other echo patterns are probably less specific to COVID-19 and are already well-described in septic shock [8]. They are probably due to the cytokine storm which injures the cardiovascular system [19]. Two different mechanisms of LV systolic dysfunction can be discussed in COVID-19. The first is much closer to septic cardiomyopathy [20], which is described as an acute injury of the heart related to cytokines [21]. In our population, LV systolic dysfunction, when present, did not involve LV dilatation, suggesting an acute injury. The second is related to the Kawasaki-like syndrome described in children and adolescents [22]. In our population, we had 2 young women, respectively 17 and 24 years of age, who developed such a syndrome with shock and severe LV failure.

Our study has some limitations. First, it was not a prospective study. However, our systematic and protocolized use of CCE for more than 20 years led us to record off-line and retrospectively most of the important information, so as to describe the echo patterns. While 14 patients did not undergo CCE, all patients who required catecholamine infusion did, at the time catecholamines were started. Second, it is a pure descriptive study, but this is the first case series reporting echocardiographic patterns in COVID-19 patients. Third, we decided not to report any longitudinal data and to limit the analysis to the first week. Indeed, due to the high ICU length of stay in these patients, we considered that after 1 week the disease progression was no longer very specific to COVID-19, but more related to the usual clinical course of critically ill patients, as ventilator-associated pneumonia or bleeding. Finally, we were unable to perform CTPA in all patients with ACP. This was mostly due to their instability. However, among those who underwent CTPA, 67% had thrombus in the pulmonary circulation.

## Conclusion

In conclusion, we report different echo patterns in COVID-19 patients admitted to the ICU, including LV systolic dysfunction, ACP, and vasoplegia. ACP was the most frequent pattern when echo was performed between day 3 and day 7 following admission in patients requiring catecholamine infusion. Echo findings also suggested that most patients had pulmonary vascular dysfunction and pulmonary hypertension. These results need to be confirmed by a large international registry.

# List Of Abbreviations

TEE, transesophageal echocardiography, TTE, transthoracic echocardiography, CCE, critical care echocardiography, ARDS, acute respiratory distress syndrome, CTPA, computed tomography pulmonary angiography, ACP, acute cor pulmonale.

## Declarations

**Ethical approval and consent to participate:** The ethics committee of the French Society of Intensive Care Medicine approved the study (CE-SRLF 20-40).

**Consent for publication:** see above ethical approval.

**Funding:** not applicable.

**Availability of data and materials:** the authors declare they keep the files containing data safely stored; these will be available to the editor on request.

**Authors 'contributions:** AVB and CC designed the study, FI and LG recorded the clinical data, AVB, CC and ST reanalyzed the echocardiographic data, AVB, CC, GG, MG, XR, PAH, AP, SC, MS, KB and RJ performed the echo studies, AVB wrote the manuscript, all authors read and approved the manuscript. All the authors have read and approved the final version of the manuscript.

**Competing interest:** the authors have read BioMed Central's guidance on competing interest and they declare no conflict of interests.

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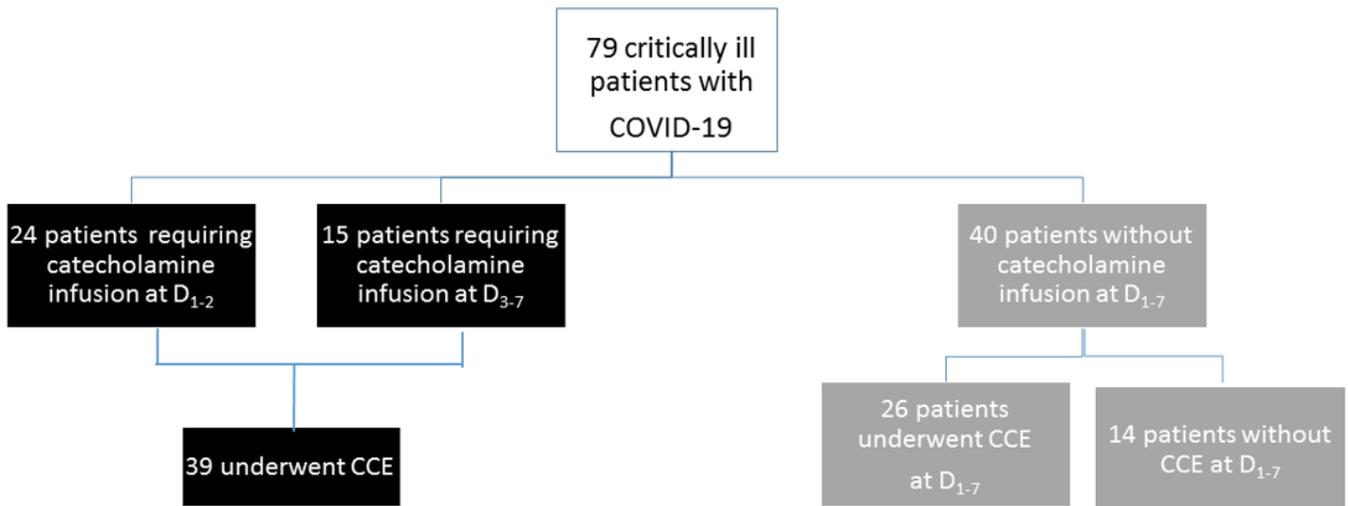
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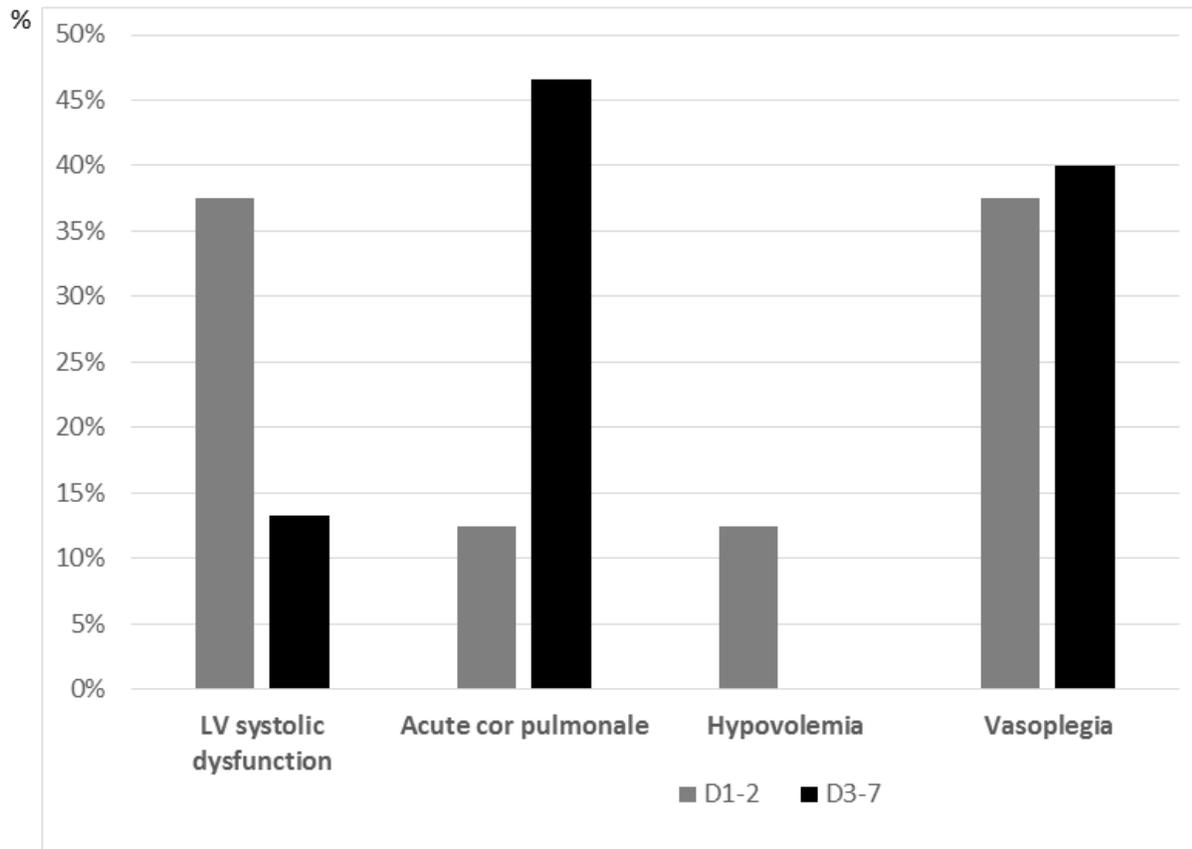
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## Figures



**Figure 1**

Flow chart of the study. CCE: critical care echocardiography, D1-7: first week of hospitalization in the ICU, D1-2: first 2 days following admission to the ICU, D3-7: period between day 3 and day 7 following admission.



**Figure 2**

Distribution in % of the main echocardiographic patterns in the 39 patients who required catecholamine infusion in the 2 periods. Grey histograms relate to the D1-2 period, while black histograms concern the D3-7 period. LV: left ventricular.

## Supplementary Files

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