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Point-of-Care Cardiac Ultrasound in COVID-19 Intensive Care Unit

Rosanna Carmela De Rosa [1,*], Antonio Romanelli [2], Roberto Colonna [1], Annunziata Minale [1], Antonio Corcione [1]

[1] Department of Anaesthesia and Intensive Care Monaldi Hospital, AORN dei Colli, Via Leonardo Bianchi, 80131 Naples, Italy; roberto.colonna@ospedalideicolli.it (R.C.); minalenunzia@virgilio.it (A.M.); corcioneanto@gmail.com (A.C.)
[2] Department of Anaesthesia and Intensive Care, AOU San Giovanni di Dio e Ruggi D'Aragona, Via San Leonardo, 84131 Salerno, Italy; antonioromanelli86@gmail.com
* Corresponding author: rosderosa.rdr@gmail.com; Tel.: +39-3386623791

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Abstract: (1) Background: Coronavirus disease 2019 (COVID-19) is associated with the development of Acute COVID-19 Cardiovascular Syndrome (ACovCS) in critically ill patients. In this case series, we evaluated the incidence of ACovCS by ultrasound in critically COVID-19 ill patients. (2) Methods: This case series included all patients with confirmed COVID-19 requiring admission to the ICU at Monaldi Hospital (AORN Ospedale dei Colli, Naples), between March 14th, 2020, and May 1st, 2020. On admission, in stable clinical conditions, an experienced and certified intensivist performed Point-Of-Care Cardiac Ultrasound (POC-CU). The exam was performed daily in every patient and repeated according to clinical evolution and intensivist's judgment during the length of stay. Ex-Novo ACovCS echocardiographic patterns were noted. (3) Results: POC-CU evaluation performed on 19 patients revealed that, on admission, five patients (26.3%) presented an echocardiographic pattern like cor pulmonale. During the length of stay, seven patients (36.8%) presented ex-Novo echocardiographic alterations, suggesting ACovCS. Pericardial effusion (26.3%), acute right impairment due to pulmonary embolism (5.3%) and acute left impairment by wall motion alteration (5.3%) were the most common findings. (4) Conclusions: Ex-Novo cardiac abnormalities shown by POC-CU were common in patients with severe COVID-19. Competence in POC-CU is essential in identifying ACovCS in COVID-ICU and clinical decision-making.

Keywords: SARS-CoV-2; COVID-19; coronavirus; point-of-care ultrasound; echocardiography; cardiovascular syndrome

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Introduction

Coronavirus Disease 2019 (COVID-19) is a Severe Acute Respiratory Syndrome due to Coronavirus-2 (SARS-CoV-2) resulting in significant morbidity and mortality. A substantial minority of hospitalised patients develop an Acute COVID-19 Cardiovascular Syndrome (ACovCS) that can manifest with a variety of clinical presentations—acute cardiac injury with cardiomyopathy, ventricular arrhythmias and hemodynamic instability—in the absence of obstructive coronary artery disease or acute pulmonary embolism (APE).

The aetiology of heart injury is uncertain but is suspected to be related to myocarditis, microvascular injury, systemic cytokine-mediated injury or stress-related cardiomyopathy, vascular thromboses.

The possibility of ACovCS requires careful cardiopulmonary monitoring and point-of-care (POC) ultrasound represents, in this scenario, a useful tool, providing a quick evaluation of the clinical picture and the therapeutic measures [1].

The lung ultrasound evaluation [2] is very important to follow respiratory damage (B-lines pattern, consolidations, pleural effusion, “white lung” picture and pneumothorax), but echocardiography [3–7] is needed to diagnose and to monitor cardiac abnormalities (acute cardiac injury, cardiomyopathy, pericarditis with pericardial effusion, arrhythmia) in critically ill patients.

As a consequence, knowledge and skill in point-of-care cardiac ultrasound (POC-CU) are essential in the management of the critical patient in the Intensive Care Unit (ICU). Daily POC-CU evaluation in ICU, performed by an experienced and certified clinician, provides useful details such as contractility, volume status, presence of cardiomyopathy or pericardial effusion, and can help the clinician to diagnose and promptly treat cardiac complications related to COVID-19 [1].

The main purpose of the present study was to evaluate the incidence of ACovCS by ultrasound in critically ill patients admitted to our COVID-19 ICU at Monaldi Hospital (AORN Ospedale dei Colli, Naples).

Materials and Methods

This case series included all the patients with confirmed SARS-CoV-2 infection (positive reverse-transcriptase polymerase chain reaction testing on nasopharyngeal swab) requiring mechanical ventilation with tracheal intubation, admitted to the ICU at Monaldi Hospital (AORN Ospedale dei Colli, Naples) between 14th March 2020, and 1st May 2020. The local ethics committee (University of Naples Luigi Vanvitelli) approved this analysis and waived the need for informed consent due to the observational nature of our study (AOC-0016235-2020).

On admission, all patients were already intubated and mechanically ventilated; they performed arterial blood gas analysis and blood chemistry tests: cell-blood count, coagulation (aPTT, PT, INR, D-dimer), liver (AST, ALT, bilirubin), kidney (urea, creatinine), heart markers (troponin I, CK-MB), inflammation and infectious markers (PCR, IL-6, procalcitonin). These tests were performed daily or repeated based on patients’ clinical changes and therapeutic adjustments. A 12-derivations ECG was performed and reviewed by an intensivist. Heart rate (HR), invasive blood pressure (IBP), SpO_2, body temperature and diuresis were monitored continuously.

All the patients were sedated by continuous infusion of propofol (2–4 mg/kg/h) or dexmedetomidine (0.8–1.5 mcg/Kg/h) and/or remifentanil (0.1–0.5 mcg/kg/min), and were connected to mechanical ventilator (Evita Drager, Germany). The infusion rates could then be adjusted stepwise to achieve the desired level of sedation. In case of mismatch to the ventilator, prone ventilation, or high plateau pressures, we used deep sedation plus

neuromuscular blockade (continuous infusion of rocuronium, 0.4–0.7 mg/Kg/h after iv bolus 0.7 mg/kg).

Based on PaO_2/FiO_2 and pulmonary compliance, two categories of patient could be identified: high-compliance patients (PaO_2/FiO_2 < 150 mmHg and compliance >50 mL/cmH_2O) and low-compliance patients (PaO_2/FiO_2 < 150 mmHg and compliance <50 mL/cmH_2O). In the second condition, we followed a protocol of protective ventilation strategy [8,9] with low tidal volumes (6 mL/kg of predicted body weight), plateau pressures (Pplat) $\leq$ 30 cmH_2O, high PEEP values titrated to maintain low driving pressures (<15 cmH_2O) and prone ventilation cycles.

For fluid management, we performed a conservative fluid strategy, obtaining a daily negative balance, to avoid an increase in "lung water", evaluated by ultrasound (B-lines, white lung).

For specific SARS-CoV-2 infection treatment, our protocol provided the administration of hydroxychloroquine, antiviral drugs (lopinavir/ritonavir, darunavir/cobicistat, remdesivir), monoclonal antibodies (tocilizumab, sarilumab) in patients with elevated inflammation markers, and glucocorticoids (methylprednisolone) in patients with Acute Respiratory Distress Syndrome (ARDS). The details are reported in Table 1.

Table 1. The table reports, in detail, the Severe Acute Respiratory Syndrome due to Coronavirus-2 (SARS-CoV-2) infection treatment protocol. Monoclonal antibodies (tocilizumab, sarilumab) were administered in patients with elevated inflammation markers, and glucocorticoids (methylprednisolone) in patients with ARDS.

Drug	Dosage
Hydroxychloroquine	200 mg, os, twice a day
Lopinavir/ritonavir	200/50 mg, os, twice a day
Darunavir/cobicistat	800/150 mg, os, once a day
Remdesivir	First dose 200 mg, then 100 mg/die, iv, once a day
Tocilizumab	A single dose of 8 mg/kg, iv, with the possibility of repeating a second administration dose after 24 h
Sarilumab	A single dose of 400 mg, sc, with the possibility of repeating a second administration dose after 24 h
Methylprednisolone	0.5 mg/kg, iv, twice a day for five days, then 20 mg twice a day for five days, finally, 10 mg twice a day

Because severe SARS-CoV-2 infection is related to high risk of thromboembolic complications [10], all patients received low-weight molecular heparin (enoxaparin), sc, following this protocol: patient's weight <60 Kg, 4000 UI, twice a day; 60–80 Kg, 6000 UI, twice a day; >80 Kg, 8000 UI, twice a day. Antiplatelet agents were administered to some patients.

Collected clinical data are reported in Table 2.

The aim of this case series is to review the incidence rate of ACovCS evaluated by POC-CU in critically ill patients with COVID-19 admitted to our ICU.

In stable clinical conditions, an experienced and certified intensivist performed POC-CU by five standard views: parasternal long-axis, parasternal short-axis, apical four-chamber, subcostal long-axis, and inferior vena cava long-axis [11]. When possible, POC-CU was performed in every patient and repeated based on patient's clinical evolution and intensivist's judgment.

POC-CU evaluation provided information about cardiovascular state on admission and showed, during the length of stay, the possible development of ACovCS by the analysis of these echocardiographic patterns:

- Acute left ventricular (LV) impairment: reduction in ejection fraction (EF), contractile anomalies, moderate-severe aortic and mitral insufficiency (respectively AI and MI);
- Acute right ventricular (RV) impairment: tricuspid annular plane excursion (TAPSE), moderate-severe tricuspidal insufficiency (TI), systolic pulmonary artery pressure (PAPs), right ventricular shape, pleural effusion, ascites;
- Pericardial effusion and possible hemodynamic involvement.

Table 2. The table reports collected clinical data.

Collected Clinical Data	
Anthropometric data	Age, sex, weight, height, BMI * and BSA †
Comorbidities	Lung disease (e.g., COPD ‡), smoking (current or former), weight excess (overweight or obese), hypertension, coronary artery disease, chronic kidney disease, metabolic and endocrinological diseases, liver disease, autoimmune disorders, solid cancer, onco-haematological disease, solid organ transplantation
On admission in ICU	PaO_2/FiO_2, HR ¶, systolic and diastolic blood pressure, ECG pattern (normal or pathologic)
During ICU recovery	Number of patients treated with hydroxychloroquine, antiviral drugs, monoclonal antibodies and glucocorticoids
	Development of cardiac rhythm alterations (e.g., atrial fibrillation)
	LOS ** and mortality rate

* Body Mass Index. † Body Surface Area (Du Bois method). ‡ Chronic Obstructive Pulmonary Disease. ¶ Heart Rate. ** Length of Stay.

The POC-CU pattern was noted as “normal” or “abnormal” on admission, and the intensivist reported the found cardiac picture. During LOS, the POC-CU was noted as “unchanged” in the absence of new cardiac patterns or, in contrary cases, the intensivist reported the shown cardiac abnormalities. Figure 1 shows the followed POC-CU protocol.

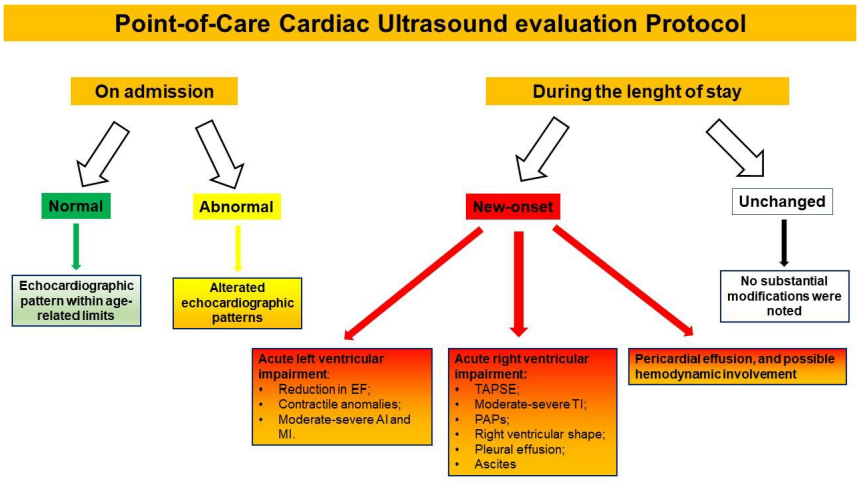

Figure 1. The figure shows the Point-of-Care Cardiac Ultrasound evaluation protocol. An experienced and certified intensivist performed echocardiographic evaluation on admission and reported the pattern as “Normal” if the echocardiographic pattern was within age-related limits, or “Abnormal” if alterations were found. During the patient’s length of stay, the echocardiographic evaluation was performed according to the patient’s clinical evolution and intensivist’s judgment. If no substantial modifications developed, the pattern was noted as “Unchanged”, or, in contrary cases, the intensivist reported the found cardiac picture.

We performed statistics with Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, USA) and XLSTAT 2020 (Addinsoft, XLSTAT statistical and data analysis solution, New York, NY, USA). We presented categorical variables as absolute numbers and percentages (%). Continuous variables were tested for normal distribution with the Shapiro–Wilk test. In the case of normal distribution, we reported data as mean ± standard deviation (SD). If not, we reported the data as median and interquartile range (IQR). We used tables to summarise the data.

Results

Twenty-two confirmed SARS-CoV-2 infected patients requiring invasive mechanical ventilation were admitted to ICU at Monaldi Hospital, between 14th March 2020, and 1st May 2020. Three patients died a few hours after admission, and POC-CU evaluation was not performed. The overall mortality rate was 72.7%.

The following analysis was based on a population of 19 patients. Table 3 reports the main population's characteristics.

Table 3. The table reports the main population characteristics. Categorical variables are presented as number or frequency (%). Continuous variables are presented as median [IQR] or mean ± SD.

Characteristic	Patients (N = 19)	
Sex-number (%)	Male	14 (73.7%)
	Female	5 (26.3%)
Age (years)	60 [54–74]	
Height (cm)	166 ± 7	
Weight (Kg)	75.0 [67.5–88.5]	
BMI (Kg m^{-2})	26.1 [25.0–31.1]	
BSA (m^2)	1.880 ± 0.211	
Comorbidities-number (%)		
Lung Disease	COPD	11 (57.9%)
	Asthma	1 (5.3%)
	Pulmonary thromboembolism	1 (5.3%)
Smoking	Current	4 (21.0%)
	Former	2 (10.5%)
Weight excess	Overweight	10 (52.6%)
	Obese	5 (26.3%)
Hypertension	14 (73.4%)	
Coronary artery disease	2 (10.5%)	
Chronic kidney disease	2 (10.5%)	
Metabolic and endocrinological diseases	Diabetes mellitus	2 (10.5%)
	Hypothyroidism	1 (5.3%)
Liver disease	0 (0%)	
Autoimmune disorders *	1 (5.3%)	
Solid cancer †	1 (5.3%)	
Onco-haematological disease ‡	2 (10.5%)	
Solid-organ transplantation ¶	1 (5.3%)	
Length of Stay (days)	10.4 ± 5.2	

* Psoriatic arthritis. † Prostate cancer. ‡ Multiple myeloma. ¶ Renal transplantation.

On admission, PaO_2/FiO_2 was 80.0 ± 37.1 mmHg, HR was 88 (IQR of 76–92) bpm, systolic and diastolic blood pressure were, respectively, 126.8 ± 14.6 and 67.9 ± 7.9 mmHg, ECG presented sinus rhythm and no pathological patterns in all patients, cardiac injury markers (troponin I, CK-MB) were negative, echocardiographic exam was normal in 14 patients (73.7%), while five patients suffered from COPD (26.3%, three male and two female) showed thickening of right ventricular wall, PAPs > 30 mmHg, dilated and non-collapsible inferior vena cava like the cor pulmonale picture. Lung ultrasound showed diffuse B-line patterns in all patients, and we strictly applied our ventilation and fluid management protocols during the LOS. The mean ± SD of LOS was 10.4 ± 5.2 days, and the mortality rate of the examined population was 68.4% (eight male and five female).

About specific SARS-CoV-2 infection treatment, all patients received hydroxychloroquine, 17 patients (89.5%) received antiviral drugs and nine patients (47.4%) were treated with monoclonal antibodies (tocilizumab seven patients, sarilumab two patients). Seven patients (36.8%) received glucocorticoids.

During the LOS, four male patients (21.0%) developed acute atrial fibrillation and one male patient (5.3%) developed torsade de point, successfully treated with defibrillation. Table 4 reports the alterations observed by POC-CU.

Table 4. The table reports the frequency of echocardiographic patterns revealed by cardiac ultrasound on admission and during the length of stay. Categorical variables are presented as number and frequency (%).

Trans-Thoracic Echocardiographic Patterns	
On Admission	
LVEF (%)	59 ± 5
TAPSE (mm)	24.0 [19.5–25.5]
PAPs (mmHg)	30.0 [28.0–40.0]
TAPSE/PAPs (mm $mmHg^{-1}$)	0.80 [0.48–0.90]
Pattern	**Patients**
Normal	14 (73.7%)
Abnormal	5 (26.3%) *
During the length of stay	
Unchanged	12 (63.1%)
Acute right ventricular impairment	1 (5.3%) †
Acute left ventricular impairment	1 (5.3%) ‡
Pericardial effusion	5 (26.3%)

* Cor pulmonale. † Acute pulmonary thromboembolism. ‡ Contractile anomalies.

During the observation time, 12 patients (63.1%) presented an unchanged POC-CU pattern, while seven patients (36.8%) presented ex-Novo alterations:

(1) One male patient (5.3%) developed acute right ventricular failure, characterised by RV dilatation and hypokinesia with a normal but hypovolemic LV and subsequent diagnostical investigations showed the presence of ex-Novo pulmonary thromboembolism;
(2) One female patient (5.3%) showed the presence of alteration of contractility (hypokinesis of the posterior interventricular septum) with ST-elevation in the right precordial derivations (STEMI) and increased troponin I levels;
(3) Five patients (26.3%, four male and one female) developed pericardial effusion without haemodynamic impairment.

No other significative alterations were noted.

Discussion

Our results, obtained from 19 patients, showed that ACovCS was common finding in critical COVID-19 patients with a frequency rate of 36.8%.

On admission, ECG showed sinusal rhythm and cardiac injury markers were negative in all subjects while in five COPD patients POC-CU showed thickening of right ventricular wall, PAPs >30 mmHg, dilated and non-collapsible inferior vena cava like cor pulmonale picture [12]. The examined population had a high incidence of COPD (57.9%), and this aspect could influence our results.

Our study population presented a mean ± SD of LOS of 10.4 ± 5.2 days in ICU. During this time, POC-CU evaluation showed that seven patients (36.8%) developed ex-Novo cardiac abnormalities. Pericardial effusion (26.3%), acute right ventricular dilatation and pulmonary hypertension due to pulmonary embolism (5.3%), and alterations in left contractility (5.3%) were reported. The overall mortality in our ICU was 72.7%, and 68.4% within the considered population.

The most common clinical finding of severe COVID-19 is the hypoxemic respiratory failure that requires mechanical ventilation. However, studies [3–7] reported that cardiac abnormalities, including acute cardiac injury, cardiomyopathy, pericarditis with pericardial effusion, arrhythmia, and sudden cardiac death, were common in critically ill patients with an increase in mortality rate.

The exact mechanism underlying cardiac alterations caused by SARS-CoV-2 infection is not fully understood, but different mechanisms can alter cardiac performance. ACovCS may be due to acute coronary syndrome, demand ischemia, microvascular ischemic injury, injury related to cytokine dysregulation or myocarditis. The pathological examination helps to clarify whether myocardial injury occurs indirectly due to systemic cytokines or directly due to viral cardiomyocyte infection or other mechanisms [13,14]. In addition, it has become clear that another hallmark of COVID-19 is coagulopathy, characterised by a predominantly thrombotic disseminated intravascular coagulation. This phenomenon can explain the high rate of sub-massive or massive APE. APE in COVID-19 patients is especially found among patients at severe or worse stages. Therefore, we should be alert to the APE events, which can be fatal in patients with COVID-19 pneumonia [15].

Regardless of the underlying mechanism, POC-CU can easily identify morphology and functional alterations. The most common findings [16] include (1) hyperdynamic cardiac function, often seen in the early stages following the systemic inflammatory response with increase of cardiac output; (2) acute stress-induced (takotsubo) cardiomyopathy with segmental contraction abnormalities and apical ballooning; (3) RV enlargement, mainly caused by increased RV afterload (alveolar and pulmonary capillary damage by inflammation, hypoxia, hypercapnia and vascular thromboses) and preload (fluid overload, mechanical ventilation, ventricular interdependence); (4) diffuse myocardial inhibition in the late stage by severe and prolonged hypoxia and inflammation.

COVID-19 patients with hypertension and diabetes have a higher probability of heart failure [17] and the ability of POC-CU to detect cardiovascular condition present on admission is crucial because it can optimise patient's clinical management with an impact on mortality. In our population, the prevalence of hypertension, CAD and diabetes were 73.4%, 10.5% and 10.5% respectively.

In our case series, pericardial effusion was the most common alteration observed by POC-CU (26.3%). Xu et al. [18], in their analysis on chest CT performed in COVID-19 patients, reported a pericardial effusion rate incidence of 1%. It seems that pericardial

effusion is a component of the myopericarditis associated with COVID-19 [19], and case reports [20,21] described the development of haemodynamic impairment by pericardial tamponade. However, in our case series, pericardial effusion was not associated with haemodynamic impairment and, contrary to myopericarditis, no raises in heart injury markers or ECG alterations were noted. Based on these data, we can suppose that pericardial effusion is related to the severity of disease and cytokine storm rather than a specific myocardial injury. Further studies on this aspect are needed.

Despite the adopted anti-coagulation protocol (enoxaparin, twice a day administration based on body weight), POC-CU showed the presence of acute right ventricular failure (right heart strain) related to APE with an incidence rate of 5.3%. Klok et al. [22] reported that APE was the major thrombotic event in COVID-19 patients in ICU, despite pharmacological thrombosis prophylaxis. In this setting, a point-of-care deep vein thrombosis study may be warranted to guide management plans such as the use of anticoagulants [1].

The incidence of left contractility alteration shown by POC-CU was of 5.3%, with an increase in heart injury markers. Acute myocardial injury is common in patients with COVID-19 and is associated with adverse prognosis [23]. With regards to the mechanism, SARS-CoV-2 infection can precipitate myocardial infarction with an oxygen supply–demand imbalance or cause virus- and cytokines-mediated myocardial injury [13]. Suggestive ischemia ECG signs must alert the clinician for prompt POC-CU execution: real-time visualisation of wall motion impairment can provide useful details, allowing for correct diagnosis and management.

Conclusion

Based on our results, Acute COVID-19 Cardiovascular Syndrome was a common finding in critical COVID-19 patients. Ex novo cardiac abnormalities involved the heart in its entirety, including the pericardium. Pericardial effusion, acute right impairment due to pulmonary embolism and acute left impairment due to wall motion alteration were the most common findings shown by POC-CU in COVID-19 ICU.

Knowledge and skill in POC-CU are essential and we strongly agree with the following statements:

(1) POC-CU performed on admission can assess the patient's cardiovascular condition;
(2) In case of sudden clinical condition worsening, POC-CU allows a rapid assessment with a prompt diagnosis of acute COVID-19-related cardiovascular complications;
(3) The quick assessment by POC-CU helps clinical decision-making about therapeutic choice, allowing real-time evaluation of the treatment.

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