Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Echocardiographic 60-day mortality markers in patients hospitalized in intensive care for COVID-19

John Jaime Sprockel Díaz[a,b,c,*], Juan Manuel Rincon[a], Manuela Alejandra Rondón López[a], Marisol Bejarano Zuleta[a], Nathaly Castellanos[a], Zulima Santofimio Saavedra[a], Hellen Cárdenas Rodríguez[a], Diego Felipe Hernandez Barrera[a], Jhon Edison Parra[a], Juan José Diaztagle Fernández[b,d]

[a] Department of Intensive Care Health Services Unit Hospital El Tunal, Integrated Health Subnet of the South, Bogotá, Colombia
[b] School of Medicine, Fundación Universitaria de Ciencias de la Salud, Internal Medicine Service Hospital de San José
[c] Institute of Research. Fundación Universitaria de Ciencias de la Salud, Bogotá, Colombia
[d] Department of Physiological Sciences, School of Medicine, Universidad Nacional de Colombia, Bogotá, Colombia

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ABSTRACT

Background: Coronavirus disease COVID-19 produces a predominantly pulmonary affection, being cardiac involvement an important component of the multiorganic dysfunction. At the moment there are few reports about the behavior of echocardiographic images in the patients who have the severe forms of the disease.
Objective: Identify the echocardiographic prognostic markers for death within 60 days in patients hospitalized in intensive care.
Methods: A single-center prospective cohort was made with patients hospitalized in intensive care for COVID-19 confirmed via polymerase chain reaction who got an echocardiogram between May and October 2020. A Cox multivariate model was plotted reporting the HR and confidence intervals with their respective p values for clinical and echocardiographic variables.
Results: Out of the 326 patients included, 153 patients got an echocardiogram performed on average 6.8 days after admission. The average age was 60.7, 47 patients (30.7%) were females and 67 (44.7%) registered positive troponin. 91 patients (59.5%) died. The univariate analysis identified TAPSE, LVEF, pulmonary artery systolic pressure, acute cor pulmonale, right ventricle diastolic dysfunction, and right ventricular dilatation as variables associated with mortality. The multivariate model identified that the acute cor pulmonale with HR= 4.05 (CI 95% 1.09 - 15.02, p 0.037), the right ventricular dilatation with HR= 3.33 (CI 95% 1.29 - 8.61, p 0.013), and LVEF with HR= 0.94 (CI 95% 0.89 - 0.99, p 0.020) were associated with mortality within 60 days.
Conclusions: In patients hospitalized in the intensive care unit for COVID-19, the LVEF, acute cor pulmonale and right ventricular dilatation are prognostic echocardiographic markers associated with death within 60 days.

Background

The virus of the Severe Acute Respiratory Syndrome – Coronavirus 2 (SARS-CoV-2) is the cause of a fast propagation disease denominated COVID-19. Its epidemiological behavior is characterized by the appearance of recurrent outbreaks exhibiting a large number of patients that develop multiorgan dysfunction that quickly overwhelms the capacity of health services due to the excessive requirement for hospitalizations in intensive care.[1] An important component in this dysfunction is the cardiac involvement that has been attributed to multiple pathophysiological mechanisms among which is the viral direct injury, hypoxemia, hemodynamic instability, systematic swelling, decrease in the expression of the Angiotensin 2 Converting Enzyme (ACE2) receptor, increase in the production of endogenous catecholamines, and toxicity of some medications prescribed for this disease.[2]

So far, the myocardial injury diagnosis has been made most of the time based on the elevation of biomarkers without cardiac imaging tests in these patients.[3] Up to now, there is no consensus on

Abbreviations: COVID-19, Coronavirus Disease – 19; TAPSE, Tricuspid annular plane systolic excursion; PASP, Pulmonary artery systolic pressure; LVEF, Left ventricular ejection fraction; ARDS, Acute Respiratory Distress Syndrome; APACHE II, Acute Physiology and Chronic Health disease Classification System II; SOFA, Sequential Organ Failure Assessment; HR, Hazard ratio; CI, Confidence interval; AUC, Area under the ROC curve; BUN, Blood urea nitrogen; SGOT, Serum glutamic-oxaloacetic transaminase; SGPT, Serum glutamic-pyruvic transaminase

* Corresponding author.
E-mail address: jjsprockel@fucsalud.edu.co (J.J.S. Díaz).

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diagnostic criteria or the use of biomarkers for this purpose. In fact, some scientific societies do not recommend the routine measurements of cardiac troponin or natriuretic peptides in patients with COVID-19, given the limited evidence of their utility to make medical decisions and the consideration that there exists a risk of improper diagnostic and therapeutical interventions based on these measurements; for this reason, routine cardiac imaging is also discouraged.[4] The guidelines from intensive care recognize troponin as a severity marker, but no recommendations are made about its measurement in critical patients.[1,5,6]

Currently, there are few reports available about the behavior of imaging, in particular echocardiographic imaging, in patients with the most serious forms of the disease.[7] Some of these works assessed the left or right ventricular dysfunction as prognostic markers of mortality; however, these studies included a mixed population of patients hospitalized in general wards and intensive care,[8-12] while the studies that focused on the population in intensive care were small reports that included a low number of events.[13-16] It was hypothesized that some prognostic markers can be identified from echocardiographic studies, so the present work aims to identify those prognostic markers for death within 60 days in patients hospitalized in intensive care based on echocardiographic findings.

Methods

An observational prospective single-center cohort study was made, which included patients hospitalized in intensive care with acute respiratory difficulty syndrome (ARDS) due to viral pneumonia by SARS-CoV-2 / COVID-19 confirmed through the real time polymerase chain reaction test (RT-PCR) in nasal swab, who got an echocardiographic study during their stay at ICU, between May and October 2020, at any of the nine intensive care units that belong to the Health Services Unit Hospital el Tunal in Bogotá, Colombia. Patients with previous conditions that determined a limitation of the therapeutical effort and pregnant women were excluded.

The cases were screened based on the daily census of ICU inpatients, all the inclusion and exclusion criteria were verified, and then the data were registered in a virtual data collection form which included the demographic variables, clinical presentation, medical history, physical examination, laboratories, and diagnostic images including the data extracted from the report for the echocardiogram performed during the ICU stay.

The clinical variables explored by the model included demographic data, medical history, vital signs, use of Angiotensin Converting Enzyme Inhibitors or Angiotensin II Receptor Antagonist, and laboratories taken during the first 72 h of hospitalization in intensive care (see supplementary Table 1 for a detailed list of variables).

The following echocardiographic markers were analyzed:

* TAPSE (as a continuous variable)
* Left ventricular ejection fraction (LVEF, as a continuous variable)
* Left ventricular diastolic dysfunction (categorized in any of its three degrees)
* Right ventricular diastolic dysfunction (defined by the presence of any of the following findings: right atrial, right ventricular or pulmonary artery dilatation, tricuspid insufficiency, interventricular septal deviation, pulmonary valvular insufficiency or McConell's sign)
* Acute cor pulmonale (defined by the presence of right ventricular dilatation plus interventricular septal deviation) [18]
* Pulmonary artery systolic pressure (PASP)
* Pericardial effusion, left ventricular contractility disorder and
* Left ventricular dilatation

The echocardiographic exam was performed by a single cardiologist using one of two portable devices: Philips HP-5500, Aloka Prosound or General Electric Vivid-E (equipped with multifrequency sector transducers). The echocardiographic measurements were done following the recommendations in the ASE and ESC guidelines[17] using a standard procedure to assess the parasternal views (long and short axis), apical (four and two chambers) as well as subcostal and suprasternal. All measurements taken for each examination were averaged over a minimum of three cardiac cycles (five to ten in case of non-sinus rhythm). In all cases the cardiologist took due precautions by washing hands and using personal protective elements, as well as the respective disinfection measures after contact with each patient.

Statistical analysis

The primary outcome was time to death within 60 days after admission in intensive care. Qualitative variables were reported with absolute frequencies and percentages whereas quantitative variables were summarized with measurements of central tendency and dispersion. To establish differences in the primary outcome as a dependent variable, a Cox proportional hazards model was developed. An univariate analysis was conducted with the different independent variables reporting their respective Hazard Ratios (HR) and 95% confidence intervals with their corresponding p values applying the Wald test. Those variables that had p smaller than 0.1 were subjected to multivariate analysis. Then, Kaplan-Meier survival curves were plotted by calculating p using the log-rank test. The analyses were performed in the R statistics software using the “survival” and “survminer” statistical packages for Cox models. The missing values were imputed by random strategy using the “Hmisc” package. The model was diagnosed using the Akaike (AIC) goodness-of-fit and Hosmer-Lemeshow tests.

Considering that the sample was obtained for convenience, the power was estimated *a posteriori* for one-sample proportion test by Binomial test from 153 patients, establishing an error alpha of 0.05 and a delta of 4%.

The present study was approved by the ethics and research committee of the Integrated Health Subnet of the South considering that an informed consent was not necessary. This work did not receive funding from any call for proposals.

Results

General description of the population

During the research period, 326 patients hospitalized in intensive care with suspected COVID-19 were screened, out of which 153 were included who had an echocardiogram report (see patient flowchart in Fig. 1). The average age was 60.7 (SD 14.1), 47 (30.7%) were female, the mean duration of symptoms before admission was 8.4 (SD 4.2) days. The most frequent comorbidities were: hypertension 58 (37.9%), diabetes 38 (24.8%), chronic pulmonary disease 32 (20.9%), and obesity 74 (48.4%). Lymphocytes were less than 1200 cells per μL in 127 (83.0%), the average CRP was 18.2 mg/L, ferritin 1264 ng/mL, LDH 1096 U/L and D-dimer 5.9 μg/mL. 67 (44.7%) had positive troponin, Table 1.

Description of outcomes

Mortality in the first 60 days occurred in 91 cases (59.5%), with an average hospital stay of 8.4 (SD: 4.2) days. Shock was present in 111 (72.5%) patients, severe ARDS (PaO2/FiO2 $<$100 mmHg) in 128 (83.7%), 142 (92.8%) required invasive ventilatory support, and 86 (56.2%) had acute kidney injury. The average APACHE II was 14.1 (SD: 6.7), SOFA was 5.2 (SD: 3.1), and CURB was 2.1 (SD: 1.2). Acute pulmonary embolism was diagnosed in 27 patients (17.6%), 16 (10.4%) patients had acute myocardial infarction and 9 (5.9%) myocarditis, Table 2.

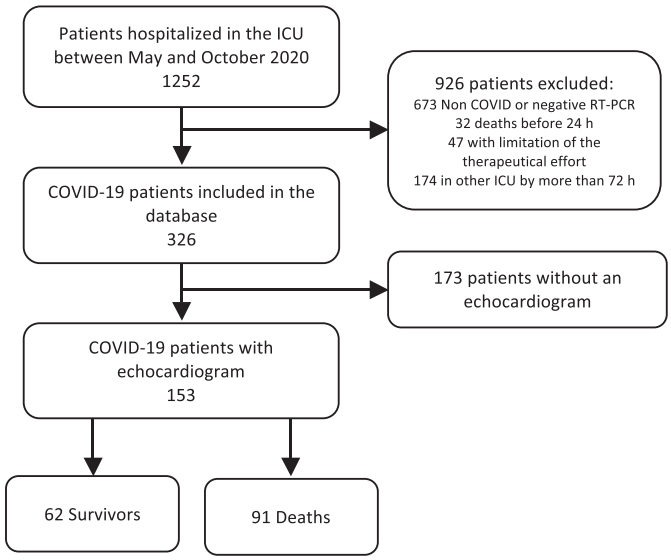

Fig. 1. Flowchart with the patient distribution.

Echocardiographic findings

Table 3 summarizes the echocardiographic findings in the patients included. The average time from ICU admission to echocardiogram was 6.8 (SD 8.3) days. The mean right ventricular ejection fraction was 37% (SD: 2.4), TAPSE decreased in 16 cases (10.4%). Right diastolic dysfunction was documented in 41 cases (26.8%). Some degree of hypertension was documented in 34 of the 48 cases in which PASP was calculated (71%). The average LVEF was 59.3% and 74 (48.4%) had some left ventricular diastolic dysfunction. In 12 (7.8%) cases there were alterations in myocardial contractility, and in 16 (10.4%) there was pericardial effusion.

Analysis of prognostic factors for in-hospital mortality

The following data were imputed: 17 for obesity, 16 for ferritin, 9 for SGPT, 6 for SGOT, and 3 for bilirubin and troponin. In the univariate analysis, the echocardiographic variables identified were: TAPSE, LVEF, pulmonary artery systolic pressure, acute cor pulmonale, right ventricular diastolic dysfunction, and right ventricular dilatation as variables related to in-hospital mortality (see supplementary Table 2). The clinical variables with significance in the univariate analysis were: age, oxygen saturation, urea nitrogen, SGTP, and troponin (see supplementary Table 3 for detailed results) and Figure 2 shows the Kaplan Meier curves relating echocardiographic variables with survival over time. The results of the multivariate analysis showed that acute cor pulmonale with HR= 4.05 (95% CI 1.09 - 15.02, p 0.037), right ventricular dilatation with HR= 3.33 (95% CI 1.29 - 8.61, p 0.013), and LVEF with HR= 0.94 (95% CI 0.89 - 0.99, p 0.020) were variables that had statistically significant association with mortality, as well as age and oxygen saturation (Table 4).

The diagnostic of the model showed a Wald test with 10 degrees of freedom out of 53, $p<0.001$, AIC 757.5, and its calibration by

Table 1
General chacteristics of the population.

Characteristic	Population of study	Survivors	Deaths	*p value*
	(*n* = 153)	(*n* = 62)	(*n* = 91)	
Female, n (%)	47 (30.7%)	21 (33.9%)	26 (28.6%)	0.604
Age (years), n (%)	60.7 (14.1)	56.1 (15.1)	63.8 (12.5)	0.001
Weight classification, n (%)			0.896	
Normal	48 (31.4%)	21 (33.9%)	27 (29.7%)	–
Low weight	1 (0.7%)	–	1 (1.1%)	–
Overwight	13 (8.5%)	3 (4.8%)	10 (11.0%)	–
Obese	74 (48.4%)	34 (54.8%)	40 (44.0%)	–
Unknown	17 (11.1%)	4 (6.5%)	13 (14.3%)	–
Comorbidities, n (%)				
Mean (SD)	1.8 (1.4)	1.9 (1.4)	1,8 (1,4)	0.485
At least one	128 (83.7%)	54 (87.1%)	74 (81,3%)	0.468
Hypertension	58 (37.9%)	25 (40.3%)	33 (36,3%)	0.735
Diabetes	38 (24.8%)	16 (25.8%)	22 (24,2%)	0.969
Chonic heart disease (except Hypertension)	21 (13.7%)	8 (12.9%)	13 (14,3%)	0.996
Chronic renal disease	8 (5.2%)	3 (4.8%)	5 (5,5%)	1.000
Smoking	38 (24.8%)	16 (25.8%)	22 (24,2%)	0.554
Chronic lung disease	32 (20.9%)	13 (21.0%)	19 (20,9%)	1.000
Duration of disease before admission in intensive care (days), median (SD)	8.4 (4.2)	8.6 (4.7)	8.2 (3.9)	0.7035
Laboratories				
White blood cell count ($\times 10^3$ cells per μL), mean (SD)	11.6 (4.5)	11.2 (4.1)	11.9 (4.8)	0.9456
Lymphocyte count ($\times 10^3$ cells per μL), mean (SD)	0.8 (0.6)	0.9 (0.7)	0.7 (0.4)	0.581
Lymphocytes less than 1,2 $\times 10^3$ cells per μL (n,%)	127 (83.0%)	53 (85.5%)	79 (86.8%)	1.000
Platelet count ($\times 10^3$ cells per μL), mean (SD)	229.2 (87.3)	250.2 (85.6)	214.8 (86.1)	0.013
Lactate (mmol/L), mean (SD)	2.0 (1.3)	1.8 (1.1)	2.2 (1.4)	0.045
Creatinine (mg/dL), mean (SD)	1.3 (1.1)	1.1 (0.8)	1.5 (1.3)	0.596
Serum glutamic-oxaloacetic transaminase (U/L), mean (SD)	124.8 (425.0)	65.5 (36.9)	164.6 (546.1)	0.094
Serum glutamic-pyruvic transaminase (U/L), mean (SD)	106.4 (270.8)	68.1 (41.1)	132.2 (347.2)	0.093
Prolongued clotting time more than 5 s (n,%)	13 (8.5%)	3 (4.8%)	10 (11.0%)	0.272
High sensitivity C-reactive protein (mg/L), mean (SD)	18.2 (14.8)	17.3 (17.0)	18.8 (13.1)	0.564
Ferritin (ng/mL), mean (SD)	1264.2 (720.7)	1233.3 (855.7)	1288.3 (599.8)	0.673
D-Dimer (μg/mL), mean (SD)	5.9 (8.2)	6.4 (9.4)	5.6 (7.3)	0.585
Lactate dehydrogenase (U/L), mean (SD)	1095.8 (933.9)	959.7 (433.1)	1188.4 (1150,8)	0.087
Positive high sensitivity cardiac Troponin I (ng/mL), mean (SD)	0.63 (2.09)	0.25 (0.71)	0,88 (2,60)	0.009
Positive high sensitivity cardiac Troponin I (n,%) *3 surviving cases did not have troponin	67/150 (44.7%)	22/59 (27.3%)	45/91 (49,4%)	0.195

SD: standard deviation.

Table 2
Description of risk scales, organ dysfunction and complications.

Characteristic	Population of study	Survivors	Deaths	*p value*
	(*n* = 153)	(*n* = 62)	(*n* = 91)	
Severity scales on day 1 of critical illness, mean (SD)				
APACHE II	14.1 (6.7)	12.4 (5.6)	15.2 (7.2)	0.006
SOFA	5.2 (3.1)	4.9 (3.1)	5.4 (3.0)	0.306
SIC	2.3 (2.0)	2.0 (0.6)	2.5 (2.5)	0.045
CURB-65	2.1 (1.2)	1.7 (1.0)	2.3 (1.2)	0.001
Organ dysfunction, n (%)				
Shock	111 (72.5%)	34 (54.8%)	77 (84.6%)	<0.001
ARDS				0.112
Severe ARDS (PaO2/FiO2: < 100 mmHg)	128 (83.7%)	48 (77.4%)	80 (87.9%)	–
Moderate ARDS (PaO2/FiO2: 100 - 200 mmHg)	20 (13.1%)	11 (17.7%)	9 (9.9%)	–
Mild ARDS (PaO2/FiO2: 200 - 300 mmHg)	5 (3.2%)	3 (4.8%)	2 (2.2%)	–
Received invasive ventilatory support	142 (92.8%)	52 (83.9%)	90 (98.9%)	0.199
Acute renal injury	86 (56.2%)	22 (35.5%)	64 (70.3%)	<0.001
Hepatopathy	23 (15.0%)	6 (9.7%)	17 (18.7%)	0.194
Coagulopathy	29 (18.9%)	6 (9.7%)	23 (25.3%)	0.027
Central nervous system dysfunction	15 (9.8%)	2 (3.2%)	13 (14.3%)	0.048
Cardiovascular complications				
Pulmonary				

thromboembolism17 (11.1%)5 (8.1%)12 (13.2%)0.467Acut myocardial infarction10 (6.5%)3 (4.8%)7 (7.7%)0.713Acute myocarditis3 (2.0%)–3 (3.3%)–Acute myocardial injury69 (45.1%)25 (40.3%)44 (48.4%)0.4154Diabetes mellitus *de novo*21 (13.7%)7 (11.3%)14 (15.4%)0.629Length of hospital stay (days), mean (SD)18.7 (10.8)32.9 (18.0)20.6 (11.3)<0.001.

SD: standard deviation, ARDS: Acute Respiratory Distress Syndrome, APACHE II: Acute Physiology And Chronic Health Evaluation, SOFA: Sequential Organ Failure Assessment, SIC: Sepsis-Induced Coagulopathy Score.

Table 3
Description of echocardiographic findings.

Characteristic	Population of study		
(*n* = 153)	Survivors		
(*n* = 62)	Deaths		
(*n* = 91)			
Time from admission to echocardiogram (days), mean (SD)	6.8 (83)	8.3 (10.8)	5.7 (5.9)
Normal echocardiogram	84 (54,4%)	38 (61.3%)	46 (50.5%)
Right ventricular ejection fraction (%), mean (SD)	37.0 (2.4)	37.2 (1.5)	36.3 (2.9)
TAPSE (mm), mean (SD)	2.0 (0.29)	2.1 (0.21)	1.9 (0.32)
TAPSE less than 16 mm	16 (10.4%)	2 (3.2%)	14 (1.0%)
Right ventricular diastolic dysfunction, n (%)			
None	112 (73.2%)	50 (80.6%)	62 (68.0%)
Septal deviation	5 (3.3%)	–	5 (5.5%)
McConell's sign	4 (2.6%)	–	4 (4.4%)
Right atrial dilatation	24 (15.7%)	6 (9.7%)	18 (19.8%)
Right ventricular dilatation	21 (13.7%)	4 (6.5%)	17 (18.7%)
Tricuspid regurgitation	25 (16.3%)	7 (11.3%)	18 (19.8%)
Pulmonary valvular insufficiency	3 (1.96%)	2 (3.2%)	1 (1.1%)
Acute cor pulmonale	5 (3.3%)	–	5 (5.5%)
Pulmonary hypertension, n (%)			
PASP could not be calculated	105 (68.6%)	46 (74.2%)	59 (64.8%)
Normal	14 (9.2%)	8 (12.9%)	6 (6.6%)
Mild (PASP 35–40 mmHg)	7 (4.6%)	2 (3.2%)	5 (5.5%)
Moderate (PASP 40–60 mmHg)	23 (15.0%)	5 (8.1%)	18 (19.8%)
Severe (PASP > 60 mmHg)	4 (2.6%)	1 (1.6%)	3 (3.3%)
Left ventricular ejection fraction (%), mean (SD)	59.3 (4.5)	59.9 (4.2)	58.9 (4.7)
Left ventricular ejection fraction less than 40%	2 (1.3%)	1 (1.6%)	1 (1.1%)
Left diastolic dysfunction	74 (48.4%)	29 (46.8%)	45 (49.4%)
Relaxation disorder (grade I)	68 (44.4%)	27 (43.5%)	41 (45.0%)
Pseudonormalization (grade II)	4 (2.6%)	2 (3.2%)	2 (2,2%)
Restrictive pattern (grade III)	2 (1.3%)	–	2 (2.2%)
Disorders of left ventricular contractility	12 (7.8%)	5 (8.1%)	7 (7.7%)
Left ventricular dilatation	5 (3.3%)	2 (3.2%)	3 (3.3%)
Pericardial effusion	16 (10.4%)	6 (9.7%)	10 (11.0%)

SD: standard deviation, PASP: pulmonary artery systolic pressure, TAPSE: Tricuspid annular plane systolic excursion.

goodness-of-fit test using Hosmer-Lemeshow obtained a Chi-square of −164.46 and $p = 1$. The *a posteriori* power calculation gave a value of 85.3%.

Discussion

Myocardial injury in patients with COVID-19 is a frequent complication in critical patients that has been associated with increased mortality,[19,20] this makes the assessment of myocardial involvement in this patient population important.[21] Without consolidated consensus, focused echocardiography becomes a valuable tool, which can influence the decision making for diagnosis or management of this group of patients.[22,23] The main result of the present study was that acute cor pulmonale, right ventricular dilatation, and LVEF had a statistically significant association with mortality within 60 days.

Few studies have been published addressing the prognostic value of echocardiography; this situation is more noticeable in the population of critical patients.[13,15] Rodriguez et al. conducted an investigation in 38 patients in a hospital in Leon (Spain); where LVEF < 50%, right ventricular dysfunction, pericardial effusion or segmental abnormalities of contractility were assessed, finding that none of them was associated with death or readmission in the follow-up period. The main limitation for these results was the small size of the sample.[13] D'Alto et al. evaluated 94 patients in two hospitals in Naples (Italy), and identified that the TAPSE/PASP ratio was an independent predictor of mortality (HR: 0.026; 95% CI: 0.01–0.579; p: 0.019), with an AUC of 0.635.[15] These variables were also identified in the univariate analysis in the results of the present work, although this association was not maintained in the multivariate analysis.

The largest study that has assessed echocardiographic findings as a prognostic factor might be the one published by the group of Kim et al. which included three hospitals in New York (USA) with 510 patients, 68% of whom came from intensive care. In this study, the adverse right ventricular remodeling resulted in a greater than 2-fold increase in the risk of mortality.[9] Barman et al. in Istanbul (Turkey), evaluated 90 hospitalized patients (32% in intensive care), documented that LVEF and right atrial diameter were independent predictors of right ventricular dilatation regardless of mortality as an outcome.[12]

Other studies that assessed only patients hospitalized in general wards coincide in showing right ventricular dilatation as a predictor of mortality.[24-26] Other markers such as decreased LVEF,[24] the presence of pulmonary hypertension,[27] TAPSE,[28] and right ventricular diastolic dysfunction[26] also showed this association. Some of these results coincide with what was found in the present study, in which right ventricular dilatation and LVEF were associated with mortality. However, it should be taken into consideration that the majority of these studies had a small number of events, a situation that limits the power of their results; it is clear that more studies are required to obtain more definitive conclusions.

In the present work, acute cor pulmonale was also associated with mortality. This condition had a low prevalence in the population taking place in five cases (3.3%), all of which were diagnosed as pulmonary embolism and died. Several recent studies have reported a prevalence of acute cor pulmonale of 22% in ARDS patients on

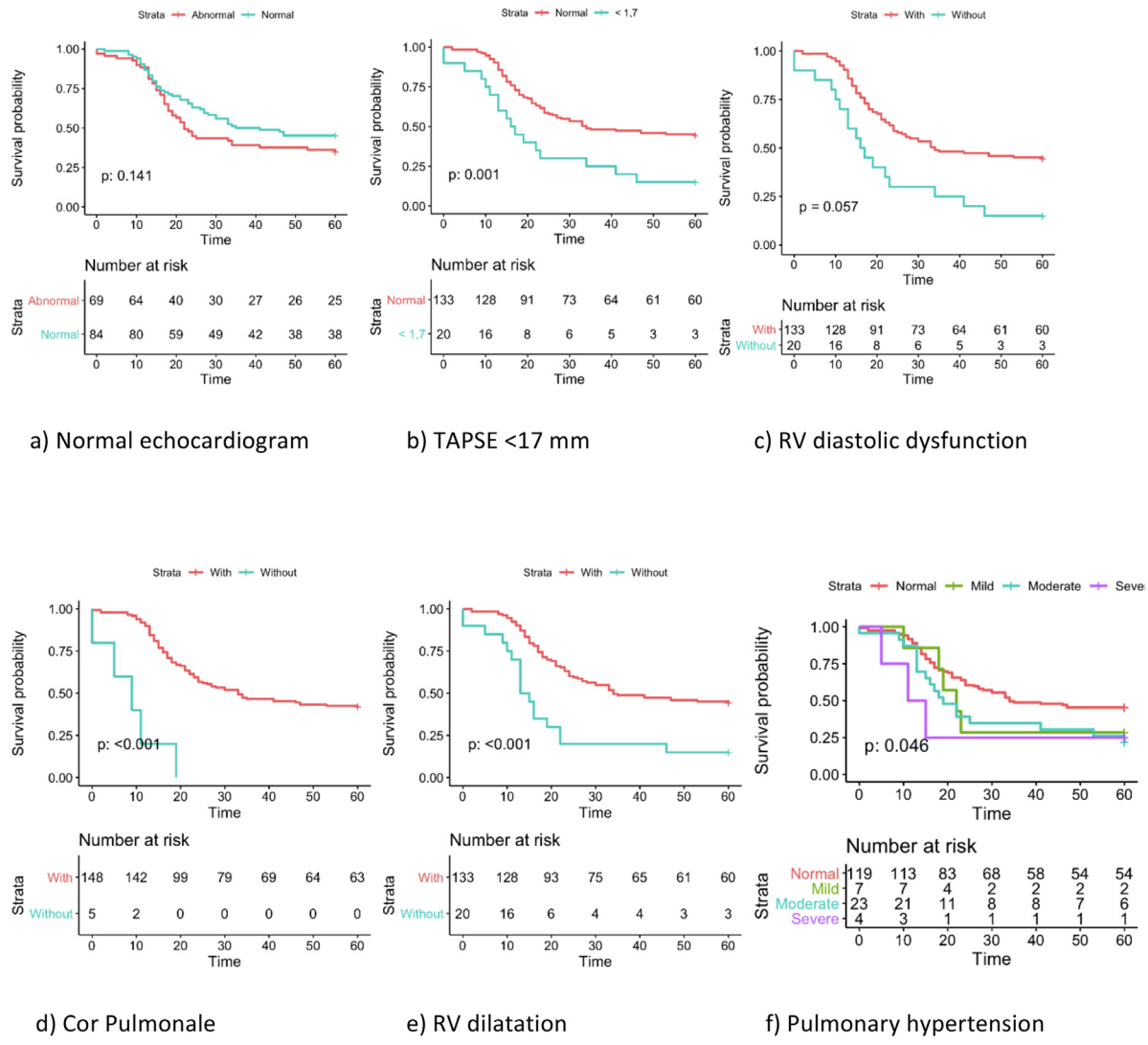

Fig. 2. Kaplan Meier survival curves for the echocardiographic variables of interest.

protective ventilation, although it was not associated with mortality.[29] A study that included patients hospitalized with COVID-19, acute cor pulmonale was reported in 2 cases (7%),[16] coinciding with the low incidence reported in the present study.

Table 4
Results of the multivariate analysis using the Cox proportional hazards model.

	Univariate analysis	Multivariate analysis		
Characteristic	HR	p	HR	95% CI	p
Echocardiographic Variables					
TAPSE	0.30	<0.001	1.27	0.42 - 3.85	0.673
Left ventricular ejection fraction	0.96	0.092	0.94	0.89 - 0.99	0.020
Right ventricular diastolic dysfunction	1.53	0.060	0.52	0.24 - 1.14	0.101
Pulmonary artery systolic pressure	1.37	0.006	1.38	0.93 - 1.97	0.111
Acute cor pulmonale	8.96	<0.001	4.05	1.09 - 15.02	0.037
Right ventricular dilatation	2.89	<0.001	3.33	1.29 - 8.61	0.013
Non-Echocardiographic Variables					
Age	1.02	0.048	1.02	1.00 - 1.04	0.038
Oxygen saturation	0.98	<0.001	0.97	0.96 - 0.99	0.001
SGPT	1.00	0.033	0.99	0.99 - 1.00	0.697
Lymphocytes	0.99	0.065	0.99	0.99 - 0.99	0.013
BUN	1.02	0.004	1.00	0.99 - 1.02	0.137
Troponine	1.24	0.009	1.15	0.96 - 1.38	0.141

TAPSE: Tricuspid annular plane systolic excursion, SGPT: Serum glutamic-pyruvic transaminase, BUN: Blood urea nitrogen, HR: Hazard ratio, CI: Confidence interval.

Echocardiographic examination in intensive care faces a number of challenges, its acquisition and interpretation are affected by mechanical ventilation, the presence of drains and bandages, suboptimal position (eg. Pronation), recent surgeries, the presence of mechanical organ supports, and pharmacological supports;[30] in addition, because it is a pathology with scientific characteristics of complex diseases, it represents great challenges for scientific analysis.[31] Also, LVEF should be used with caution in critical patients, particularly in those with shock due to the use of vasoactive drugs, and right ventricular diastolic function is more likely to be affected in critical patients.[32]

The present study has several limitations. A selection bias cannot be ruled out either, since the target population were patients who got an echocardiogram, which was performed on those with an unfavorable clinical course. The single-center nature of the present study limits the external validity of the results. Although a previous calculation of the sample size was not carried out, the power obtained was adequate for the validation of the conclusions obtained. The acquisition of echocardiograms in critical patients with COVID-19 represents a challenge in terms of biosafety for the specialist performing the examination; in the present study, the images were acquired by a single specialist and were not recorded or confronted with the concept of a peer, which would have been desirable to improve the quality of the data. Finally, although some data were imputed, this procedure was performed on few variables, making it unlikely to have a major impact on the results obtained.

The present study is a Latin American cohort of critical patients, being one of those with the highest number of events reported to date in echocardiographic studies that assessed prognosis; which is a strength, since it allowed further exploration into echocardiographic variables as a prognostic factor.

Conclusion

In patients hospitalized in the intensive care unit for COVID-19, the presence of right ventricular dilatation and acute cor pulmonale (defined as right ventricular dilatation associated with paradoxical septal motion) were echocardiographic markers independently associated with death within 60 days.

Authors' contributions

John Sprockel and Diego Hernandez conceived and designed the study. Juan Rincon, Manuela Rondón, Marisol Bejarano, Nathaly Castellanos, Zulima Santofimio, and Hellen Cárdenas contributed to data acquisition. John Sprockel conducted the statistical analysis. John Sprockel, Diego Hernandez, John Parra, Juan Rincon, and Juan Diaztagle prepared the paper. All the authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Availability of data and materials

All data generated and/or analyzed during this study are available from the corresponding author on reasonable request conditioned by its review by the institutional ethics and research committee.

Ethics approval and consent to participate

The present study was approved by the ethics and research committee of the Integrated Health Subnet of the South considering that it was not necessary to obtain an informed consent.

Consent for publication

Not applicable.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2021.12.007.

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