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.

Heart & Lung 57 (2022) 1–6

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.com

Influence of right ventricular structure and function on hospital outcomes in COVID-19 patients

Jozef Oweis, MD[a,*], Annie Leamon, BS[a], Ali H. Al-Tarbsheh, MD[a], Katharine Goodspeed, BSMS[a], Ciril Khorolsky, MD[b], Paul Feustel, PHD[d], Usman Naseer, MBBS[a], Isam Albaba, MBBS[a], Sai Anoosh Parimi, MBBS[a], Boris Shkolnik, MD[c], Anupama Tiwari, MD[c], Amit Chopra, MD[c,#], Mikhail Torosoff, MD[b,#]

[a] Department of Internal Medicine, Albany Medical Center, 43 New Scotland Avenue, Albany, New York, 12208, United States of America
[b] Department of Cardiology, Albany Medical Center, 43 New Scotland Avenue, Albany, New York, 12208, United States of America
[c] Department of Pulmonary and Critical Care Medicine, Albany Medical Center, 43 New Scotland Avenue, Albany, New York, 12208, United States of America
[d] Department of Neuroscience and Experimental Therapeutics, 43 New Scotland Avenue, Albany, New York, 12208, United States of America

ARTICLE INFO

Article History:
Received 19 January 2022
Revised 7 August 2022
Accepted 8 August 2022
Available online 11 August 2022

Keywords:
Right ventricular dilatation
Right ventricular dysfunction
COVID-19
Echocardiogram

ABSTRACT

Background: The impact of the right ventricular (RV) structure and function on the in-hospital outcomes in patients with COVID-19 infection has not been rigorously investigated.
Objectives: The main aim of our study was to investigate in-hospital outcomes including mortality, ICU admission, mechanical ventilation, pressor support, associated with RV dilatation, and RV systolic dysfunction in COVID-19 patients without a history of pulmonary hypertension.
Methods: It was a single academic tertiary center, retrospective cohort study of 997 PCR-confirmed COVID-19 patients. One hundred ninty-four of those patients did not have a history of pulmonary hypertension and underwent transthoracic echocardiography at the request of the treating physicians for clinical indications. Clinical endpoints which included mortality, ICU admission, need for mechanical ventilation or pressor support were abstracted from the electronic charts.
Results: Patients' mean age was 68+/-16 years old and 42% of the study population were females. COPD was reported in 13% of the study population, whereas asthma was 10%, and CAD was 25%. The mean BMI was 29.8+/-9.5 kg/m2. Overall mortality was 27%, 46% in ICU patients, and 9% in the rest of the cohort. There were no significant differences in co-morbidities between expired patients and the survivors. A total of 19% of patients had evidence of RV dilatation and 17% manifested decreased RV systolic function. RV dilatation or decreased RV systolic function were noted in 24% of the total study population. RV dilatation was significantly more common in expired patients (15% vs 29%, $p = 0.026$) and was associated with increased mortality in patients treated in the ICU (HR 2.966, 95%CI 1.067–8.243, $p = 0.037$), who did not need require positive pressure ventilation, IV pressor support or acute hemodialysis.
Conclusions: In hospitalized COVID-19 patients without a history of pulmonary hypertension, RV dilatation is associated with a 2-fold increase in inpatient mortality and a 3-fold increase in ICU mortality.

Introduction

Right ventricular dysfunction (RVD) manifesting with RV dilatation and/or decreased RV systolic function has been reported in 8% to 52% COVID-19 patients.[1-3] However, it remains unclear whether RVD is a marker of COVID-19 lung injury causing acute RV pressure overload or whether RVD is independent of the lung disease process.[4] Pathophysiology of RVD in COVID-19 is likely multifactorial and, in some patients, may reflect acute RV pressure overload due to acute lung disease, while in others it may be due to direct myocardial viral injury, hypoxia, inflammatory response, and/or autoimmune injury,

Abbreviations: RV, right ventricle; RVD, right ventricular dysfunction; BMI, body mass index; COPD, chronic obstructive pulmonary disorder; CAD, coronary artery disease; CRP, C-reactive protein; ALT, alanine transaminase; LDH, lactate dehydrogenase; ICU, intensive care unit; PPV, positive pressure ventilation; LV, left ventricle; RVEDA, right ventricular end-diastolic area; LVEDA, left ventricular end-diastolic area.; RVFAC, right ventricular fractional area capacity; RVS', right ventricular S prime; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TV, tricuspid valve

* Corresponding author.
E-mail address: oweisj@amc.edu (J. Oweis).
# Dr. Chopra and Dr. Torosoff are both senior authors and contributed equally to this paper.

https://doi.org/10.1016/j.hrtlng.2022.08.007
0147-9563/

or it may be a manifestation of the pre-existing lung or heart disease unrelated to COVID-19 infection.[5, 6]

Understanding the RVD influence on COVID-19 clinical course and outcomes is evolving. In two recent meta-analyses, one involving 1450 COVID-19 patients, 50% mechanically ventilated, reported a 3.1-fold increase in mortality associated with decreased RV systolic function and a 2.4-fold increase associated with RV dilatation.[6] On the contrary, in another meta-analysis of 3944 COVID-19 patients, 66% in the ICU setting, RV dilatation and/or depressed RV systolic function was more prevalent but was not definitely associated with increased mortality.[7] Differences in results may be due to the patient selection, co-morbidities, various pathophysiology of RVD, or other yet unidentified factors, which highlights the need for further studies on this subject. The role of RVD in COVID-19 requires investigation to better understand the disease process, design optimal management practices, and ensure proper resource utilization while providing the best possible care.[8]

Methods

The study was approved by the Institutional Review Board. It was a retrospective cohort study of 997 consecutive adult COVID-19 patients treated at a single tertiary care academic medical center between March 1st, 2020, and January 10th, 2021. COVID-19 was diagnosed via real-time reverse transcription-polymerase chain reaction (RT-PCR) from a nasopharyngeal swab. All study patients underwent transthoracic echocardiography at the request of the treating physicians for clinical indications as part of the standard medical care during hospitalization. Patients with pulmonary hypertension were excluded. The remaining 194 patients comprised the study cohort.

The following data were collected for each patient: a) demographics including age, sex, and ethnicity; b) comorbidities including coronary artery disease, chronic pulmonary disease, diabetes mellitus, hypertension, and cancer; c) admission laboratory parameters including procalcitonin, ferritin, C-reactive protein (CRP), and D-dimer levels; d) echocardiographic findings including RV size and systolic function, estimated RV systolic pressure, RV fractional area change, LV ejection fraction; and e) outcomes including in-hospital mortality, need for ICU admission, positive pressure ventilation, acute hemodialysis, or IV pressor support.

LV and RV targeted transthoracic echocardiograms were performed according to the American Society of Echocardiography recommendations in the ICAEL-accredited hospital non-invasive imaging laboratory by the certified trained sonographers and permanently stored off-line for the subsequent interpretation.[4] We have used General Electric E9 and E95 workstations to perform our studies. Post-processing was performed on commercially available software DigiView v.3.8.6.2. SP5 Build 165, Intelerad Medical Systems, WA, USA. Cardiac function and structure were assessed in parasternal long and short axis, apical 2 and 4 chambers, and subcostal views. RV Size, RV systolic function, RV fractional area change (RVFAC), RV and LV end-diastolic (ED) areas and RVEDA/LVEDA ratio, RV systolic pressure (RVSP), tricuspid annular plane systolic excursion (TAPSE), and tissue Doppler RV systolic velocity (RVs') were recorded. LV and RV dimensions and function assessment and all echocardiographic measurements were performed following 2015 American Society of Echocardiography recommendations for cardiac chamber quantification by echocardiography in adults.[9] Echocardiograms were initially interpreted by the National Board of Echocardiography (NBE) certified cardiologists independently from the study at the time when the test was performed for clinical indications. The subsequent study-related echocardiographic assessment was performed off-line by the cardiology fellow (CK) and independently confirmed by an NBE-certified study cardiologist (MT).

Categorical data were presented as frequency and percentage with a chi-square test of significance unless the expected value in any cell was less than five, in which case Fisher's exact test was used. Normally distributed continuous data were presented as mean plus and minus the standard deviation with significance assessed by a *t*-test. Non-normal data were presented as a median and interquartile range with a non-parametric Mann-Whitney test for significance. Analysis was performed with R (version 3.6.1) and Minitab (v.19) commercially available statistical software packages.

Results

The study cohort included 194 COVID-19 patients who did not have a history of pulmonary hypertension and/or RV dysfunction and underwent echocardiographic evaluation.

The baseline clinical characteristics of patients are shown in Table 1. The mean age of the cohort was 68+/−16 years old, 42% of the patients were females, BMI was 29.8+/−9.5 kg/m^2. Chronic obstructive pulmonary disease was present in 13% of patients, asthma in 10%, and almost 25% of the patients had a history of coronary artery disease. There were no significant differences in co-morbidities between expired patients and the survivors. Overall mortality was 27% (52/194), 46% (43/93) in patients requiring ICU treatment, and 9% (9/101) in the rest of the cohort. The expired patients were more likely to be treated in the ICU, required positive pressure ventilation, acute hemodialysis, or IV pressors. These clinical care endpoints were subsequently included in the logistic regression analysis.

The echocardiographic parameters are shown in Table 2. A total of 19% (36/194) patients had evidence of RV dilatation and 17% (33/194) manifested decreased RV systolic function. RV dilatation with decreased RV systolic function was noted in 12% (23/194), and RV dilatation or decrease RV systolic function were noted in 24% (46/194) of patients. RV dilatation was significantly more common in expired patients (15% vs 29%, p = 0.026) and was included in the logistic regression analysis of hospital outcomes. RVEDA/LVEDA ratio was also significantly increased in expired patients (0.520 +/−0.123 vs. 0.596+/−0.156, p = 0.011). However, as RVEDA/LVEDA is reflective of RV dilatation, it was not included in the logistic regression analysis together with RV dilatation. RVFAC was numerically decreased in expired patients and RVFAC<35% was more common in expired patients (37 vs. 26%), but this difference was not statistically significant. Estimated RV systolic pressure was significantly higher in expired patients and severe TV regurgitation, though overall uncommon, was also noted more frequently in expired patients. Given the low prevalence of severe TR (3%), this variable was not used in the logistic regression analysis.

Table 3 shows that the need for ICU admission, positive pressure ventilation, acute hemodialysis, IV pressors, and RV dilatation were significantly associated with COVID-19 hospital mortality in the univariate analysis. However, in a multivariate analysis, only the need for positive pressure ventilation remained a statistically significant predictor of hospital mortality and there was a strong trend towards increased hospital mortality in patients with RV dilatation.

When stratified by each significant predictor or mortality, as presented in Table 4, RV dilation was associated with increased mortality in patients who required ICU admission and in patients who did not require hemodialysis with a similar strong trend noted in patients who did not require positive pressure ventilation or IV pressor support.

Discussion

Understanding of RV dysfunction (RVD) effects on COVID-19 clinical course and outcomes is evolving. With the reported prevalence of RVD in COVID-19 patients ranging from 8% to 52%,[1-3] RVD is increasingly recognized as an important indicator of COVID-19 severity and

Table 1
Demographic, clinical characteristics, and hospital outcomes.

Total patients: n (%)	Total Cohort 194 (100)	Alive 142 (73.2)	Expired 52 (26.8)	p-value
Gender, female: n (%)	81 (42.0)	58 (40.8)	23 (44.2)	0.672
Age, years old: mean (SD)	67.6 (15.8)	66.4 (16.1)	70.7 (14.4)	0.090
Race, non-whites: n (%)	63 (32.5)	48 (33.8)	15 (28.8)	0.514
BMI, kg/m2: mean (SD)	29.8 (9.5)	29.3 (9.5)	31.1 (9.6)	0.248
COPD: n (%)	25 (12.9)	18 (12.7)	7 (13.5)	0.885
Asthma: n (%)	19 (9.8)	14 (9.9)	5 (9.6)	0.960
Diabetes mellitus: n (%)	60 (30.9)	41 (28.9)	19 (36.5)	0.306
Hypertension: n (%)	118 (60.8)	84 (59.2)	34 (65.4)	0.431
CAD: n (%)	48 (24.7)	33 (23.2)	15 (28.8)	0.423
Atrial fibrillation: n (%)	36 (18.6)	24 (16.9)	12 (23.1)	0.327
Smoking, past or current: n (%)	53 (27.3)	38 (26.8)	15 (28.8)	0.773
Hemoglobin, mg/dL: mean (SD)	12.6 (8.8)	13.1 (10.3)	11.6 (2.6)	0.318
Peak troponin, ng/L: mean (SD)	1.2 (5.5)	1.1 (6.1)	1.4 (3.7)	0.784
CRP, mg/L: mean (SD)	118.5 (129.3)	107.9 (133.1)	142.2 (118.2)	0.144
ALT, IU/L: mean (SD)	32.6 (37.1)	30.1 (31.4)	38.9 (48.4)	0.171
LDH, IU/L: mean (SD)	320.2 (171.9)	284.7 (120.2)	403.7 (237.1)	<0.001
Ferritin, ng/mL: mean (SD)	681.4 (1002.5)	492.0 (643.2)	1132.5 (1470.1)	<0.001
D-Dimer. Ng/mL: mean (SD)	7.7 (21.2)	6.0 (18.5)	11.5 (26.1)	0.164
ICU admission: n (%)*	93 (47.9)	50 (35.2)	43 (82.7)	<0.001
Mechanical ventilation: n (%)	56 (28.9)	26 (18.3)	30 (57.7)	<0.001
Bi-PAP: n (%)	15 (7.8)	5 (3.5)	10 (19.2)	<0.001
CPAP: n (%)	7 (3.6)	1 (0.7)	6 (11.5)	<0.001
Positive pressure ventilation: n (%)*	68 (35.1)	30 (21.1)	38 (73.1)	<0.001
Acute hemodialysis: n (%)*	12 (6.2)	4 (2.8)	8 (15.4)	0.001
IV pressors: n (%)*	49 (25.3)	20 (14.1)	29 (55.8)	<0.001
Pulmonary Embolism: n (%)	4 (2.1)	3 (2.1)	1 (1.9)	0.934

* Variables used in logistic regression analysis.

adverse outcomes associated with severe COVID-19.[10] The exact mechanisms of RVD in COVID-19 remain under investigation and it continues to be unclear whether RVD is a marker of COVID-19 lung injury causing acute RV pressure overload or whether RVD is independent of the lung disease process.[4] It has been suggested that primary RVD may be due to direct myocardial injury from COVID-19 viral myocarditis, hypoxia, inflammatory response, and/or autoimmune injury.[5, 6] Role of RV dysfunction in COVID-19 requires further investigation not only to understand the disease process but also to design optimal management practices. As obtaining an echocardiographic evaluation involves resource utilization and exposes imaging personnel to COVID-19, it is important to define the patient population in whom RV assessment is clinically meaningful.[8] Our study extends current knowledge of COVID-19 effects on RV function and outcomes by examining patients without a history of pulmonary hypertension.

Table 2
Echocardiographic parameters.

Total patients: n (%)	Total Cohort 194 (100)	Alive 142 (73.2)	Expired 52 (26.8)	p-value
LV end-diastolic dimension, cm: mean (SD)	4.5 (0.9)	4.6 (0.9)	4.4 (0.9)	0.195
LV ejection fraction <35%: n (%)	13 (6.7)	8 (5.6)	5 (9.6)	0.326
RV dilatation: n (%)*	36 (18.6)	21 (14.8)	15 (28.8)	0.026
RVEDA/LVEDA ratio: mean (SD)	0.540 (0.135)	0.520 (0.123)	0.596 (0.156)	0.011
RV with depressed contractility: n (%)	33 (17.1)	21 (14.8)	12 (23.1)	0.174
RVFAC,%: mean (SD)	38.9 (7.8)	39.1 (7.7)	38.4 (8.3)	0.721
RVFAC <35%: n (%)	30 (28.6)	20 (25.6)	10 (37.0)	0.259
TAPSE, mm: mean (SD)	18.2 (4.5)	18.6 (4.1)	17.2 (5.5)	0.239
RVS', cm/s: mean (SD)	14.4 (3.1)	14.4 (2.8)	14.6 (3.9)	0.681
RV dilated **and** depressed: n (%)	23 (11.9)	13 (9.2)	10 (19.2)	0.055
RV dilated **or** depressed: n (%)	46 (23.7)	29 (20.4)	17 (32.7)	0.075
RV systolic pressure, mmHg: mean (SD)	34.9 (10.8)	33.7 (10.2)	28.0 (12.0)	0.031
Severe TV regurgitation: n (%)	4 (2.6)	1 (0.9)	3 (7.0)	0.037

* Variables used in logistic regression analysis.

In our study, RV dilatation or systolic dysfunction were noted in approximately 20% of imaged COVID-19 patients without a history of pulmonary hypertension. Very few published studies in COVID-19 patients compared current and prior echocardiograms. Similar to our study, in a 510-patient 3-hospital New York city registry reported by *Kim et al.*, when compared to pre-COVID-19 echocardiograms available in 14%, current RV dilation was noted in 55.2% vs. historic 38.8% (a 16% difference, $p = 0.06$) and RV dysfunction in 28.2% vs. 12.8% ($p = 0.21$), or any adverse RV remodeling of 74.5% vs. 45.5% (a 29% difference, $p = 0.002$).[11] In the 120-patients study of London North West University Healthcare NHS Trust by *Bioh et al.*, when compared to the historic echocardiograms, new RV dysfunction was noted in 50%, which is significantly higher than observed in our study.[12] Along with a high incidence of RV dysfunction, authors reported elevated RVSP>=50mm Hg in 26%, which was significantly more prevalent to less than 5% noted in our study, which probably explains the significantly higher incidence of RV dysfunction in their study, as compared to ours.[12] In a prospective 100 patient study from Israel by *Szekely et al.*, 39% of patients had RV dilatation or RV systolic dysfunction at baseline and an additional 12% exhibited new RV dysfunction when the echocardiogram was repeated for evaluation of clinical deterioration.[13] Accounting for the differences between studies with regards to the patient mix and COVID-19 severity, our findings, and prior results suggest that new RV dysfunction may be found in approximately 20% of COVID-19 patients undergoing echocardiographic evaluation for clinical indications.

In our study, RV dilatation was associated with more than 30% overall mortality, compared to 20% in the rest of the cohort. Given the variation in published study populations and recorded endpoints, apprising prior reports on the effects of RV dysfunction on COVID-19

Table 3
Predictors of hospital mortality.

Parameter	Univariate model		Multivariate model	
	HR, 95% CI	p-value	HR, 95% CI	p-value
ICU admission	8.8, 3.963–19.502*	<0.001	2.3, 0.738–7.358	0.149
Positive pressure ventilation	10.1, 4.867–21.100*	<0.001	3.7, 1.218–11.084*	0.021
Acute hemodialysis	6.3, 1.802–21.837*	<0.004	2.4, 0.527–10.646	0.261
IV pressors	7.7, 3.731–15.853*	<0.001	1.9, 0.714–4.833	0.205
RV dilatation	2.336, 1.095–4.985*	0.028	2.3, 0.938–5.716	0.069

* Detrimental effect, increases mortality. For example, the need for ICU admission increased hospital mortality risk by factor of 8.8 with the 95% confidence interval of 3.963–19.502 and a p-value of <0.001.

Table 4
RV dilatation as mortality predictor in patients stratified by clinical parameters.

	RV dilatation as a predictor of mortality in patients with "X" parameter		RV dilatation as a predictor of mortality in patients without "X" parameter	
Parameter "X":	HR, 95% CI	p-value	HR, 95% CI	p-value
ICU admission	2.966, 1.067–8.243*	0.037	0.696, 0.081–6.012	0.742
Positive pressure ventilation	1.8, 0.537–5.938	0.344	3.3, 0.989–11.231	0.052
Acute hemodialysis†	–	–	2.326, 1.053–5.184*	0.037
IV pressors	1.524, 0.389–5.968	0.545	2.702, 0.969–7.535	0.057

* Detrimental, increases mortality. For example, in patients with the need for ICU admission, RV dilatation increased hospital mortality risk by factor of 2.966 with the 95% confidence interval of 1.067–8.243 and a p-value of 0.037.
† Due to paucity of cases, effects of RV dilatation could not be assessed in patients who required acute hemodialysis.

outcomes and comparing them with our results is difficult. Two recent meta-analyses cited similar problems. In one 1450 patients meta-analysis from USA, Mexico, China, UK, Italy, and Germany, where 50% of patients required mechanical ventilation, decreased RV systolic function was associated with 3.1-fold and RV dilatation with a 2.4-fold increase in mortality.[6] In another, larger meta-analysis, summarizing 29 studies including 3944 predominantly (68%) ICU patients, RV dilatation and/or depressed RV systolic function was not definitely associated with increased mortality.[7] It is likely that with a wide range of co-morbidities and varying COVID-19 severity, simple pooling and averaging of the data may lead to results that are difficult to interpret.

For the purposes of this discussion, we have selected and tabulated (Table 5) prior relevant reports where there was sufficient data for between-study comparisons, including RV dysfunction, need for mechanical ventilation, and mortality rates.[2, 11, 12, 14-21] To simplify

Table 5
Review of reported morbidities, clinical variables, and outcomes by prior investigators.

	Imaged patients, N (%)	Mortality	RV Dilatation	Decreased RV contractility	ICU	PPV	IV pressors
Pagnesi et al.[2]	200 (95)	13	15	–	13	31	–
Soulat-Dufour et al.[21]	445 (15)	15	12	16	35	–	–
Karagodin et al.[17]	870 (100)	22	33	29	46	27	18
Norderfeldt et al.[19]	67 (88)	22	40	65	100	92	62
Current study	*194 (19)*	*27*	*19*	*17*	*48*	*35*	*25*
Bioh et al.[12]	120 (100)	28	42	50	35	41	–
Kim et al.[11]	510 (100)	32	35	15	68	60	61
Pimentel et al.[20]	163 (100)	34	10	–	66	39	20
Mahmoud-Elsayed et al.[18]	73 (95)	38	46	25	–	82	58
Garcia-Cruz et al.[16]	82 (100)	41	28	27	100	79	–
Chotalia et al.[15]	171 (64)	59	49	51	–	100	–
Belligund et al.[14]	25 (30)	63	35	–	100	84	–

	Pulmonary Embolism	Males	Age, median or mean+/-SD	DM	HTN	CAD or CHF	COPD or Asthma
Pagnesi	8	66	62	19	42	13	6
Soulat-Dufour	12	66	69+/−16	29	60	29	8
Karagodin	–	56	60	20	42	7.3	–
Norderfeldt	16	94	58	–	–	–	–
Current study	*2*	*58*	*67+/−16*	*31*	*61*	*25*	*23*
Bioh	–	67	67+/−17	49	55	33	31
Kim	–	66	64+/−14	41	63	–	13
Pimentel	–	59	64+/−16	37	71	14	5
Mahmoud-Elsayed	7	78	59+/−13	36	42	9	–
Garcia-Cruz	–	62	–	44	–	–	–
Chotalia	–	77	59 (49–67)	–	–	–	4
Belligund	–	95	71+/−9	55	82	–	16

*Studies sorted by reported mortality.
†Numbers represent proportions, unless stated otherwise.

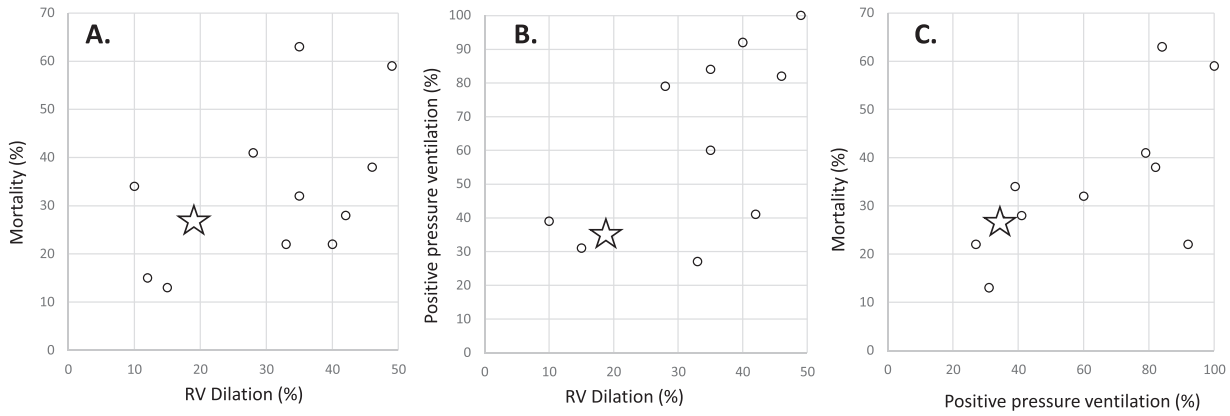

Fig. 1. AssociationbetweenICUadmissions,positivepressureventilation,andRVdilatation. In the studies with available data endpoints, including current one (star), visual assessment reveals strong positive correlation between RV dilatation and mortality (Panel A), RV dilatation and positive pressure ventilation (Panel B), and positive pressure ventilation and mortality (Panel C).[2, 11, 12, 14-21]

the comparison between our study and the previously published reports, prior studies were sorted by the reported hospital mortality. Accounting for differences in study populations and reported endpoints, our findings agree with prior reports. Furthermore, when examining available data, across the spectrum of the published studies, there appears to be a robust positive correlation between RV dilatation and COVID-19 mortality (Fig. 1, panel A), RV dilatation, and positive pressure ventilation (Fig. 1, panel B), and COVID-19 mortality and positive pressure ventilation (Fig. 1, panel C). Given the low prevalence of LV systolic dysfunction and/or left-sided valvular disease, a strong correlation between RV dysfunction and the need for positive pressure ventilation suggests that RV dysfunction is likely a secondary phenomenon, but nonetheless an important predictor of mortality. In addition to revealing a correlation between RV dilatation and COVID-19 mortality, close examination of the tabulated data and figures also reveals significant variation in the prevalence of RV dysfunction and mortality between studies, which explains inconclusive and discrepant results of the reported meta-analyses, as some studies had low and some studies had a high prevalence of both endpoints, likely driven by patient populations, evolving COVID-19 care experience, and available therapeutic options.

Intuitively, besides RV parameters, other factors reflecting overall disease severity, e.g., ICU admission, positive pressure ventilation, IV vasopressor use, and/or acute hemodialysis are expected to be associated with increased mortality in acutely ill patients, and they were in the univariate, but not in the multivariate analysis. Only positive pressure ventilation continued to be an important predictor of mortality when ICU admission, acute hemodialysis, IV pressors, and RV dysfunction were accounted for. This leads to the conclusion that the overall prognosis in COVID-19 patients requiring positive pressure ventilation largely depends on the management of pulmonary involvement and systemic oxygenation, while other therapeutic interventions aimed at other morbidities are probably bringing the expected benefits and do not significantly and independently contribute to mortality. This notion is confirmed by the observation when, despite preserved LV systolic function, there is a need for venovenous extracorporeal membrane oxygenation (ECMO) mortality in patients with RV dilatation is extremely high, 73% vs. 35% in patients with normal RV dimensions.[10] In our study, despite significantly milder than reported in the ECMO study disease severity, still there was a strong trend (p = 0.069) for RV dilatation in predicting mortality in the multivariate analysis along with positive pressure ventilation.

Finally, like prior investigators, we have collected and reported multiple RV structure and function parameters, including RV Size, RV systolic function, RV fractional area change, RV/LV end-diastolic area ratio, RV systolic pressure, tricuspid annular plane systolic excursion, and tissue Doppler RV systolic velocity (RVs'). Other investigators also assessed even more labor-intensive RV strain and RV 3D ejection fraction.[22-24] However, our data indicates that a simple endpoint of RV dilatation is the most robust predictor of outcomes in COVD-19 patients undergoing echocardiograms for clinical indications. This endpoint is also easiest to obtain and interpret, qualitatively or quantitatively.[9] Given the high degree of COVID-19 transmissibility and the need to minimize personnel exposure and risk of infection, it is prudent to conduct an echocardiographic evaluation in the patients who will benefit the most and to limit studies to only absolute necessary imaging.[4, 8] This evaluation of RV dimensions in COVID-19 can be successfully done with the point-of-care ultrasound minimizing exposure yet obtaining critical clinical information.[8, 16] From that perspective, when stratified by individual clinical care components, echocardiographic evaluation of RV dimensions appears to be most important in determining the prognosis of the patients admitted to the ICU, especially if their COVID-19 severity does not require positive pressure ventilation, dialysis, and IV pressors.

We present the results of a large single academic institution cohort study of COVID-19 patients who received multidisciplinary state-of-the-art care by experienced nurses, residents, fellows, and attending physicians. Best diagnostic and treatment practices were followed. The study sample is large and allows adequate statistical analysis. Our findings meaningfully add to the existing knowledge. Our study emphasized the impact of the RV structure and function on in-hospital mortality of patients with COVID-19 infection. Therefore, we recommend the use of the bedside echocardiogram as an initial assessment to determine the prognosis and management plan in patients with COVID-19 infection. Additionally, our study gives rise to future research to investigate the effect of early administration of certain medications, such as Epoprostenol, in COVID-19 patients with RVD.

There are several limitations to our study. This was a single-center study, but our findings are biologically plausible and in accord with prior reports. We did not exclude patients without a historic echocardiogram. However, putting our study design and findings in the context of clinical care, the majority of patients with acute pathology typically lack prior cardiac testing, which is true not just for COVID-19 but for any other study of acute disease. Lastly, echocardiograms were obtained for clinical indications and our cohort might have been composed of patients with more aggressive disease as those patients were more likely to receive more detailed workup. Therefore, our findings should be applied only to the patients who undergo transthoracic echocardiograms for clinical indications.

Conclusions

In a nearly 1000 patient cohort where approximately 20% of COVID-19 patients underwent echocardiographic evaluation for clinical indications and did not have a history of pulmonary hypertension, RV dilatation or depressed RV systolic function were detected in 20%, with 20% mortality in patients without RV abnormalities and 30% mortality in patients with RV abnormalities. Echocardiographic evaluation of RV dimensions is important in determining the prognosis of the COVID-19 patients admitted to the ICU.

Declaration of Competing Interest

None.

CRediT authorship contribution statement

Jozef Oweis: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft. **Annie Leamon:** Conceptualization, Methodology, Investigation, Data curation, Writing – original draft. **Ali H. Al-Tarbsheh:** Conceptualization, Methodology, Investigation, Data curation, Writing – review & editing. **Katharine Goodspeed:** Conceptualization, Methodology, Investigation, Data curation, Writing – review & editing. **Ciril Khorolsky:** Methodology, Investigation, Data curation, Writing – review & editing. **Paul Feustel:** Data curation. **Usman Naseer:** Data curation. **Isam Albaba:** Data curation. **Sai Anoosh Parimi:** Data curation. **Boris Shkolnik:** Writing – review & editing. **Anupama Tiwari:** Writing – review & editing. **Amit Chopra:** Conceptualization, Methodology, Investigation, Data curation, Supervision, Project administration, Writing – review & editing. **Mikhail Torosoff:** Conceptualization, Methodology, Investigation, Data curation, Supervision, Project administration, Writing – review & editing.

Acknowledgment

We are indebted to our superb sonographers who obtained echocardiographic images analyzed in this study and to the supporting staff, nurses, interns, residents, fellows, and attending physicians who cared for the patients included in this study. Their courage, dedication, technical skills, and clinical acumen allowed excellent patient care and made this study possible.

References

1. Moody WE, Mahmoud-Elsayed HM, Senior J, et al. Impact of right ventricular dysfunction on mortality in patients hospitalized with COVID-19, according to race. *CJC Open*. 2021;3:91–100. https://doi.org/10.1016/j.cjco.2020.09.016.
2. Pagnesi M, Baldetti L, Beneduce A, et al. Pulmonary hypertension and right ventricular involvement in hospitalised patients with COVID-19. *Heart*. 2020;106:1324–1331. https://doi.org/10.1136/heartjnl-2020-317355.
3. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol*. May 2020;17:259–260. https://doi.org/10.1038/s41569-020-0360-5.
4. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE statement on protection of patients and echocardiography service providers during the 2019 novel coronavirus outbreak: endorsed by the American College of Cardiology. *J Am Soc Echocardiogr*. 2020;33:648–653. https://doi.org/10.1016/j.echo.2020.04.001.
5. Lan Y, Liu W, Zhou Y. Right Ventricular Damage in COVID-19: association Between Myocardial Injury and COVID-19. *Review*. 2021;8. https://doi.org/10.3389/fcvm.2021.606318. 2021-February-16.
6. Paternoster G, Bertini P, Innelli P, et al. Right ventricular dysfunction in patients with COVID-19: a systematic review and meta-analysis. *J Cardiothorac Vasc Anesth*. 2021;35:3319–3324. https://doi.org/10.1053/j.jvca.2021.04.008.
7. Messina A, Sanfilippo F, Milani A, et al. COVID-19-related echocardiographic patterns of cardiovascular dysfunction in critically ill patients: a systematic review of the current literature. *J Crit Care*. 2021;65:26–35. https://doi.org/10.1016/j.jcrc.2021.05.010.
8. Kirkpatrick JN, Hull SC, Fedson S, Mullen B, Goodlin SJ. Scarce-resource allocation and patient triage during the COVID-19 pandemic: JACC review topic of the week. *J Am Coll Cardiol*. 2020;76:85–92. https://doi.org/10.1016/j.jacc.2020.05.006.
9. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28:1–39. https://doi.org/10.1016/j.echo.2014.10.003. e14.
10. Lazzeri C, Bonizzoli M, Batacchi S, et al. Persistent right ventricle dilatation in sARS-CoV-2-related acute respiratory distress syndrome on extracorporeal membrane oxygenation support. *J Cardiothorac Vasc Anesth*. 2021. https://doi.org/10.1053/j.jvca.2021.08.028.
11. Kim J, Volodarskiy A, Sultana R, et al. Prognostic utility of right ventricular remodeling over conventional risk stratification in patients with COVID-19. *J Am Coll Cardiol*. 2020;76:1965–1977. https://doi.org/10.1016/j.jacc.2020.08.066.
12. Bioh G, Botrous C, Howard E, Patel A, Hampson R, Senior R. Prevalence of cardiac pathology and relation to mortality in a multiethnic population hospitalised with COVID-19. *Open Heart*. 2021;8. https://doi.org/10.1136/openhrt-2021-001833.
13. Szekely Y, Lichter Y, Taieb P, et al. Spectrum of cardiac manifestations in COVID-19: a systematic echocardiographic study. *Circulation*. Jul 28 2020;142:342–353. https://doi.org/10.1161/CIRCULATIONAHA.120.047971.
14. Belligund P, Lee D, Balasubramaniam M, et al. Right ventricle dilation detected on point-of-care ultrasound is a predictor of poor outcomes in critically ill patients with COVID-19. *Fed Pract*. 2021;38:396–401. https://doi.org/10.12788/fp.0177.
15. Chotalia M, Ali M, Alderman JE, et al. Right ventricular dysfunction and its association with mortality in coronavirus disease 2019 acute respiratory distress syndrome. *Crit Care Med*. 2021;49:1757–1768. https://doi.org/10.1097/CCM.0000000000005167.
16. Garcia-Cruz E, Manzur-Sandoval D, Rascon-Sabido R, et al. Critical care ultrasonography during COVID-19 pandemic: the ORACLE protocol. *Echocardiography (Mount Kisco, NY)*. 2020;37:1353–1361. https://doi.org/10.1111/echo.14837.
17. Karagodin I, Carvalho Singulane C, Woodward GM, et al. Echocardiographic correlates of in-hospital death in patients with acute COVID-19 infection: the World Alliance Societies of Echocardiography (WASE-COVID) Study. *J Am Soc Echocardiogr*. 2021;34:819–830. https://doi.org/10.1016/j.echo.2021.05.010.
18. Mahmoud-Elsayed HM, Moody WE, Bradlow WM, et al. Echocardiographic findings in patients with COVID-19 pneumonia. *Can J Cardiol*. 2020;36:1203–1207. https://doi.org/10.1016/j.cjca.2020.05.030.
19. Norderfeldt J, Liliequist A, Frostell C, et al. Acute pulmonary hypertension and short-term outcomes in severe Covid-19 patients needing intensive care. *Acta Anaesthesiol Scand*. 2021;65:761–769. https://doi.org/10.1111/aas.13819.
20. Pimentel SLG, Nascimento BR, Franco J, et al. Bedside echocardiography to predict mortality of COVID-19 patients beyond clinical data: data from the PROVAR-COVID study. *Rev Soc Bras Med Trop*. 2021;54: e03822021. https://doi.org/10.1590/0037-8682-0382-2021.
21. Soulat-Dufour L, Fauvel C, Weizman O, et al. Prognostic value of right ventricular dilatation in patients with COVID-19: a multicentre study. *Eur Heart J Cardiovasc Imaging*. 2021. https://doi.org/10.1093/ehjci/jeab067.
22. Lassen MCH, Skaarup KG, Lind JN, et al. Echocardiographic abnormalities and predictors of mortality in hospitalized COVID-19 patients: the ECHOVID-19 study. *ESC Heart Fail*. 2020. https://doi.org/10.1002/ehf2.13044.
23. Li Y, Li H, Zhu S, et al. Prognostic value of right ventricular longitudinal strain in patients with COVID-19. *JACC Cardiovasc Imaging*. 2020;13:2287–2299. https://doi.org/10.1016/j.jcmg.2020.04.014.
24. Zhang Y, Sun W, Wu C, et al. Prognostic value of right ventricular ejection fraction assessed by 3D echocardiography in COVID-19 patients. *Front Cardiovasc Med*. 2021;8: 641088. https://doi.org/10.3389/fcvm.2021.641088.