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Relation between Right Ventricle Echocardiographic Parameters and Severity of Corona Virus Disease 19

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ABSTRACT

Background: COVID-19 is a complex and evolving multi-organ disease with cardiovascular effects that will not be fully understood while the pandemic is ongoing. This study evaluate the relationship between the severity of COVID 19 and right ventricular function parameters using 2D echocardiography. **Patients and methods:** This cross sectional study was conducted on one hundred hospitalized COVID-19 PCR-positive patients with mild, moderate, or severe symptoms who were admitted to AL-MOKATTAM Health Insurance Hospital. Patients were subjected to detailed history taking, clinical examinations, chest CT and transthoracic echocardiography. **Results:** All echocardiographic findings of RV show significant difference from mild to severe Covid 19 manifestations ($p < 0.05$). There is a significant relation between echocardiographic parameters of the RV and CT severity score ($p < 0.05$). Correlation coefficient (r) between tricuspid annular plane systolic excursion (TAPSE) showed a significant negative correlation ($r = -0.1539$, $p = 0.038$). There is also significant negative correlation between chest CT severity score and each of TASV and RV FAC (%) ($p < 0.05$). A significant positive correlation was found between chest CT severity score and & RV MPI ($p < 0.05$). **Conclusion:** RV dysfunction increases in COVID-19 patients with respiratory symptoms as their clinical severity increases. RV FAC identified RV dysfunction in 29% of patients. There is a significant positive correlation between CT severity Score and RV MPI, however there is significant negative correlation between CT severity score, RV FAC, TAPSE and TASV.

Key words: COVID 19, RV dysfunction, Severity of COVID 19.

Introduction

Ever since COVID-19 was formally classified as a pandemic by the World Health Organization (WHO), it has spread quickly and wreaked havoc across the globe. Over 50 million individuals had been infected as of November 11, 2020, and over one million people have died from the virus [1].

Acute respiratory distress syndrome (ARDS) to mild upper respiratory symptoms are among the well-known respiratory system effects of SARS-CoV-2 [2].

Nonetheless, a substantial body of research indicates that this illness targets the cardiovascular system. According to Gackowski, COVID-19 appears to have a variety of effects on the cardiovascular system, exhibiting symptoms that vary from asymptomatic increases of cardiac biomarkers to cardiovascular collapse and cardiac arrest [3].

Research indicates that approximately 20% of this group experiences myocardial damage, and that up to 40% of people who pass away have myocardial injury, whether or not respiratory failure is present [4].

Echocardiography is an affordable and widely accessible method of assessing the anatomy and functionality of the heart. A focused examination yields valuable information that might influence treatment decisions in critically ill patients [5].

Patients with COVID-19 have been reported to have acute cor pulmonale, or right heart failure due to acute pulmonary hypertension, which is brought on by an acute pulmonary embolism or adult respiratory distress syndrome (ARDS). Individuals with COVID-19 are susceptible to ARDS development. Patients with COVID-19 who are critically unwell frequently experience venous thromboembolism, which can include pulmonary embolism and severe deep vein thrombosis [6].

Recently, important data about the echocardiographic signs and symptoms of COVID-19 have been made available. elevated afterload, resulting in dysfunction or failure of the right ventricle. Thus, we postulated that hypoxemia in COVID-19 could affect RV performance by presenting as a distinct hemodynamic phenotype without an increase in afterload. In order to enable further medical intervention and prevent the development of complications, this study was conducted to assess relation between severity of COVID 19 and right ventricular function parameters using 2D echocardiography.

Patients and Methods

The study was conducted on one hundred hospitalized COVID-19 PCR-positive patients with mild, moderate, or severe symptoms who were admitted to AL-MOKATTAM Health Insurance Hospital between April 2021 and April 2022.

Patient was admitted to the hospital after a 72-hour PCR test revealed a positive COVID-19 infection, male or non-pregnant female adult who was at least 18 years old when they enrolled, and patients with any length of symptoms indicative with COVID-19, including at least one of the following (imaging-based radiographic infiltrations (chest x-rays, CT scans, etc.); OR $SpO_2 \leq 94\%$ in room air or needing extra oxygen) were included in the study. Patients with past history of acute myocardial infarction or acute arrhythmia or a 72-hour notice of expected hospital release or transfer to a different hospital that is not a study site or patients with pulmonary embolism were excluded from the study.

A positive reverse-transcriptase polymerase chain reaction test for COVID19 respiratory syndrome coronavirus in a respiratory tract sample verified the diagnosis of COVID-19 infection in all patients. The Chinese National Health Commission released recommendations for the diagnosis and treatment of COVID-19 on February 18, 2020, and they were followed for the patients with mild, moderate, and severe cases who were recruited in this study [7].

- Mild illness: People who do not have dyspnea, shortness of breath, or abnormal chest imaging but who exhibit any of the many COVID-19 signs and symptoms (such as fever, cough, sore throat, malaise, headache, muscular pain, nausea, vomiting, diarrhea, and loss of taste and smell).
- Moderate illness: People with an oxygen saturation determined by pulse oximetry (SpO_2) $\geq 94\%$ on room air at sea level and signs of lower respiratory disease during clinical examination or imaging.

• Severe illness: People with a respiratory rate more than 30 breaths per minute, lung infiltrates greater than 50%, arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) ratio less than 300 mm Hg, or SpO_2 less than 94% on room air at sea level. (COVID19 treatment guidelines panel. Corona virus disease 2019 (COVID-19) Treatment Guidelines. National institute Health. Available at https://www.covid19treatmentguidelines.nih.gov/).

Patients were subjected to detailed history taking and clinical examinations. The patients were assessed (0-25) by two expert radiologists according to the level of lobar involvement in chest CT as shown in table 1. These gradings were utilized to construct 3 COVID-19severity groups. A thorough transthoracic echocardiography performed by cardiologists skilled in the recording and interpretation of echocardiograms using the same device (GE Vivid S6).

Table 1: CT Severity Score [8].

CT Severity level	CT severity Score	CT score and lung lobe
Mild	**0-6**	**5-25%**
Moderate	**7-18**	**26-49%**
Severe	**18-25**	**>50%**

Typical transthoracic echocardiogram in two dimensions: Using, the echocardiographic investigation was conducted. Ultrasonic apparatus: This investigation employed a GE vivid S6 with a 3S-RS Phased Array Transducer operating at 3.5 GHz. The following techniques were used to evaluate the right ventricle:

I. RV measurements: RV dimensions were calculated using an apical four-chamber image with a focus on the RV.RV dilatation is often indicated by a diameter more than 41 mm at the base and greater than 35 mm at the mid-level in the RV-focused image. Maximum transversal dimension = basal RV linear dimension (RVD1) The level of the papillary mussels at the end diastole in the basal one-third of the RV flow is equal to the transverse RV diameter in the middle third of the RV flow, or almost midway between the maximal basal diameter and the apex.

II. Right ventricular systolic function: The following methods were used to assess RV systolic function [9].

1-TAPSE (trans annular plane systolic excursion): It was measured by M-mode echocardiography with the cursor optimally align along the direction of the tricuspid lateral annulus in the apical four-chamber view (normal value>17 mm),

2-RV 2D FAC (fractional area change):from RV-focused apical four chamber view, RV FAC(%)=100× (EDA-ESA)/EDA. While tracing the RV area, care must be taken to include the trabeculae in the RV cavity (normal value>35%).

3. RV MPI(Right Ventricular Myocardial performance index): Pulsed wave TDI was placed at the lateral tricuspid annulus to measure the peak velocities of IVC (IVC max), S wave (S max), E′, A′ waves and E′/A′ ratio also the duration of IVC, IVR, time to peak of IVC, S wave duration were measured. RV MPI: MPI=(IVCT+IVRT/)ET.

4. Lateral annular velocity (RV S’): using right ventricular dimension using right ventricle basal diameter measured in the apical 4-chamber view (10).RV systolic dysfunction is defined as S′ velocity < 9.5 cm/sec by TDI.

In compliance with the most recent recommendations [10]. The following actions were made to reduce the possibility of infection: All echocardiography tests were conducted at the hospital's authorized COVID-19 admitted patient's bedside. In order to reduce the possibility of infection transmission, these echocardiography scanners were reserved for the critical care unit dedicated for COVID-19. Airborne precautions, consisting of N-95 respirator masks, fluid-resistant gowns, two sets of gloves, head coverings, eye shields, and shoe covers, were used as personal protection during the echocardiographic recordings. To minimize exposure and contamination, no ECG monitoring was used during imaging, and all measurements were done offline.

Statistical analysis

The statistical software for the social sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA) was used to code and input the data. For quantitative data, the mean, standard deviation, median, and interquartile range were used; for categorical data, the frequency (count) and relative frequency (%) were used. The non-parametric Mann-Whitney test was used to compare numerical variables. We used the Chi square (2) test to compare categorical data. When the anticipated frequency is less than 5, an exact test was employed instead. Pearson correlation test to assess relation between study variables and P-values less than 0.05 were regarded as statistically significant.

Ethical approval: Every case-sharing participant in the study provided his or her consent. Any patient who was mulling over taking part in this research was given a thorough explanation of all the steps, presented in a manner they could fully comprehend. The Ethical Committee Council of Suez Canal University approved the study. The study was done in compliance with the Declaration of Helsinki, which is the World Medical Association's code of ethics for studies for humans.

Results

This study included 100 COVID 19 patients with mean ±SD age of 63.13 ± 9.4 years and 72 males (72%) and 28 females (28%). The participants' ages ranged from 33 to 86 years.

In figure 1, mild respiratory involvement and including 8 patients, moderate respiratory involvement and including 76 patients and severe respiratory involvement and including 16 patients.

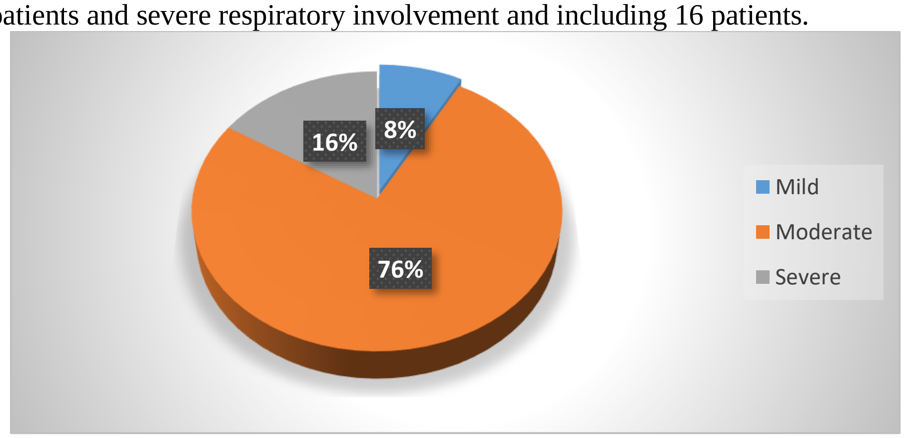

Figure 1: Severity grading distribution among the study patients.

Table 2 showed a statistically significant difference (p <0.05) is observed in all right ventricular echocardiographic findings between moderate and severe Covid-19 manifestations. Deteriorations in RV function are linked to an increase in the severity of clinical state among Covid-19 patients.

Table 2: Relation between echocardiographic parameters of the right ventricle and clinical manifestations of COVID 19 patients.

Echocardiographic parameters	Covid 19; manifestation (mean ±SD)			Significance	
	Mild (8)	Mod (76)	Severe (16)	F	P
RV basal D(mm)	31.45 ± 5.17	38.2 ± 5.32	42.91 ± 4.92	1.71	0.047*
RV mid D (mm)	27.33 ± 4.67	32.09 ± 3.86	40.52 ± 4.27	3.42	0.008*
TAPSE (mm)	24.84 ± 4.58	21.55 ± 3.47	17.82 ± 3.36	7.201	0.001*

S` TAV (msec)	20.64 ± 4.45	15.98 ± 4.34	10.78 ± 4.13	-9.87	0.000*
RV MPI	0.16 ± 0.09	0.25 ± 0.11	0.41 ± 0.12	25.4	0.000*
RV FAC (%)	41.69 ± 3.72	35.78 ± 3.07	28.41 ± 2.99	7.28	0.001*
CT Severity Score	6±0.8	12±5	20±2	5.986	0.002*

F: ANOVA test, P <0.05: significant.

While TASV and FAC% were significant only in the severe stage of Covid-19 symptoms, TASPSE was dramatically reduced in both moderate and severe cases as shown in table 3.

Table 3: Correlation coefficient and regression analysis between important echocardiographic parameters of the right ventricle and clinical manifestations of COVID 19 patients.

RV Echocardiographic parameters	COVID 19; manifestation					
	Mild (8)		Mod (76)		Severe (16)	
	r	P	r	P	r	P
TAPSE (mm)	-0.2387	0.061	-0.1667	0.042*	-0.1952	0.037*
TASV (mm)	0.0824	0.097	0.1414	0.055	0.1798	0.041*
RV FAC (%)	-0.0612	0.118	-0.2383	0.062	-0.1699	0.044*

r: Pearson correlation test, P <0.05: significant.

Table 4 showed that, ll right ventricular echocardiographic results demonstrate a statistically significant difference (p <0.05) between the moderate and severe Covid 19 CT severity scores. RV function declines are linked to an increase in Covid19 patients' severity scores.

Table 4: Relation between echocardiographic parameters of the right ventricle and CT severity score in COVID 19 patients.

Echocardiographic parameters	COVID 19; CT severity score (mean ±SD)			Significance	
	Mild N (6) **(<7)**	**Moderate N** (76) **(7-18)**	**Severe** N (18) **(>18)**	**F**	**P**
RV basal D (mm)	35.24 ± 2.96	38.12 ± 5.18	44.83 ± 2.78	2.59	0.048*
RV mid D (mm)	29.24 ± 2.96	32.12 ± 5.18	38.83 ± 2.78	2.59	0.048*
TAPSE (mm)	20.77 ± 2.91	19.89 ± 3.695	13.41 ± 1.98	4.136	0.009*
S` TAV (msec)	17.15 ± 3.18	15.99 ± 4.34	7.5 ± 0.787	33.65	0.000*
RV MPI	0.209 ± 0.053	0.252 ± 0.111	0.478 ± 0.03	9.987	0.000*
RV FAC (%)	37.51 ± 2.767	35.89 ± 3.695	31.93 ±2.506	5.312	0.005*

F: ANOVA test, P <0.05: significant.

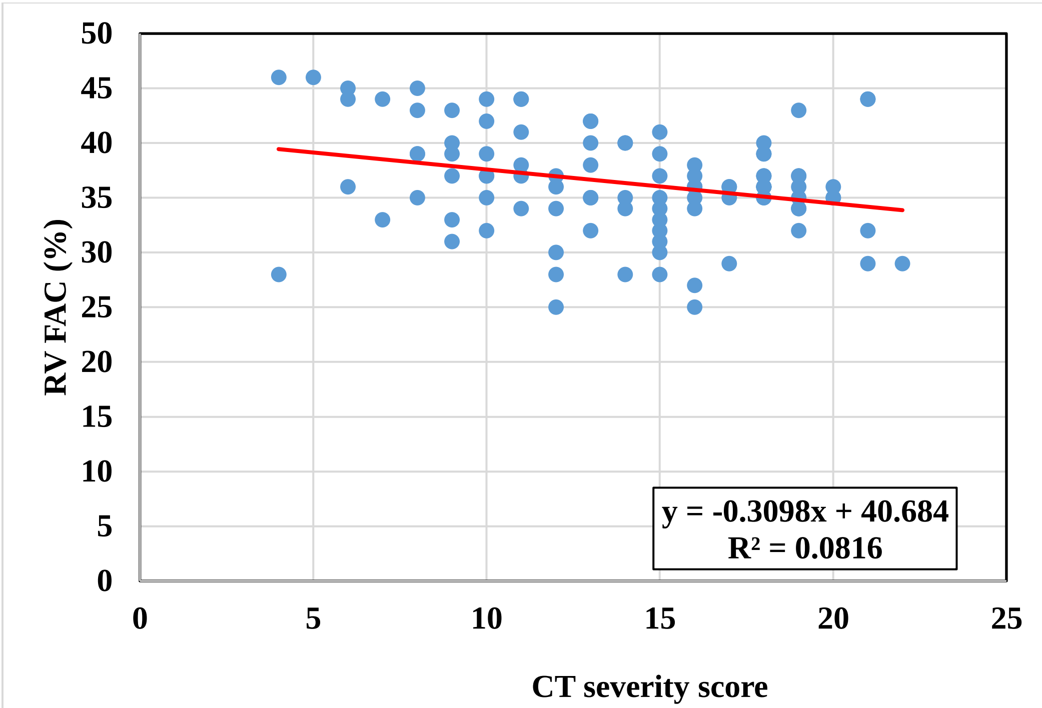

Figure 2: Correlation coefficient (r) between chest CT severity score and RV FAC (%).

There was a significant negative correlation between the two parameters (r = - 0.2857, p =0.018).

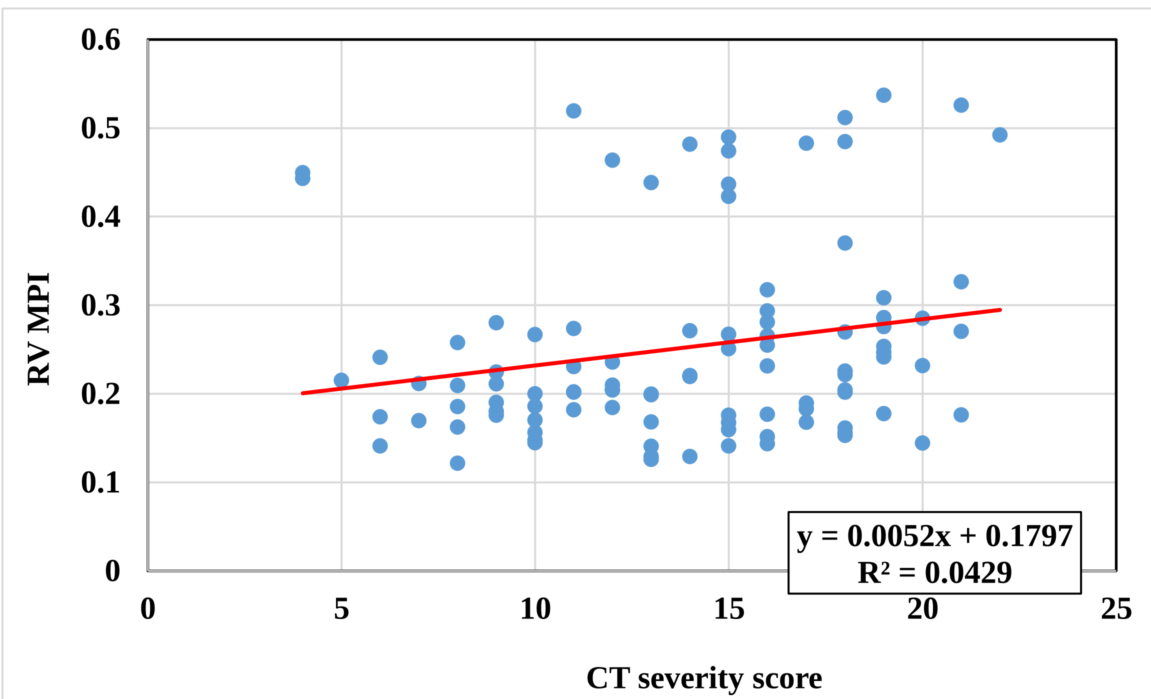

Figure 3: Correlation coefficient (r) between chest CT severity score and RV MPI.

There was a significant positive correlation between the two parameters (r = 0.20712, p =0.035).

Discussion

Several studies have indicated a high correlation between mortality and RV failure in patients with COVID-19 [11–13].

So this study was conducted to assess relation between severity of COVID 19 and right ventricular function parameters using 2D echocardiography. The study included 100 Covid-19 patients, with a mean age of 63.13 ± 9.404 years (range: 33 – 86 years) and 72 men (72%) and 28 females (28%). With the exception of oxygen saturation, which was below average, all test results are within normal levels.

All RV echocardiographic result in the present study demonstrates a significant difference ($p < 0.05$) between moderate and severe Covid 19 symptoms. Patients with Covid-19 have more severe clinical statuses as their RV function deteriorates. In Covid 19 patients, there is a statistically significant correlation ($p < 0.05$) between the RV's echocardiographic characteristics and the CT severity score.

Of the 282 hospitalized Covid-19 patients investigated by Brennan et al.[14] who underwent an echocardiography and were on mechanical ventilation, 61 (21.6%) showed indications of at least moderate RV dysfunction, mostly by TAPSE. The number of patients with significant RV dysfunction was just 6, or 2.1%. There was a report of moderately or significantly dilated RV visual fields in about 41% of the patients.

According to research by Abella et al. [15] TAPSE ≤17 is linked to a higher requirement for intensive care hospitalization and a worsening of COVID-19 illness.

TASPSE was shown to be considerably lower in Covid-19 symptoms that were moderate to severe in our study, but TASV and FAC% were significant only in the severe stage.

The baseline echocardiographic research conducted by Rothe et al. [16] showed that the mean RV base diameter ranged from 32 to 48 mm, while the mean TAPSE was 19.7 mm, with a range of 14 to 28 mm. Although there is a considerable association between RV basal dimensions and PASP, TAPSE, a measure of RV systolic functions, did not reveal a statistically significant correlation to PASP. This result may be explained by the variety of variables that affect TAPSE readings, including RV wall motion index, ischemic heart failure etiology, and LV systolic functions. Another thing to consider is how the intensity of the TR jet affects the repeatability of TAPSE; severe TR introduces uncertainty when using TAPSE to evaluate RV systolic functions.

There is a substantial negative connection ($p < 0.05$) between the chest CT severity score and each of the TAPSE and TASV in the current investigation. RV FAC (%) and the chest CT severity score correlated significantly negatively ($p < 0.05$). The RV MPI and chest CT severity score correlated significantly positively ($p < 0.05$).

RV FAC and RV VTI were both linked to RV size by RVEDAi (RV end diastolic area index) and RVESAI (RV end systolic area index), according to research by Bleakley et al.[17]. On the other hand, TAPSE only associated with RVESAI ($p = 0.33$), but RVS' did not correlate with either RV size by RVEDAi on univariate regression ($p = 0.24$) or with RVESAI ($p = 0.11$). RV VTI and RV FAC decrease showed a high correlation, whereas RVS did not. Although the correlation was not as strong statistically, TAPSE was associated with lower RV FAC. The study indicates that RV free wall strain may be a predictor of RV dysfunction in COVID-19 patients in a subset by demonstrating a relationship between RV (FAC) and RV end-systolic area index (RVESAI). Nevertheless, as this is only one study, additional investigation is required to corroborate this result and ascertain the function of RV free wall strain in COVID-19 patients as a predictor of RV dysfunction. When determining the likelihood of RV dysfunction in COVID-19 patients, it is critical to take into account all relevant variables, including underlying medical disorders such diabetes mellitus.

RV FAC/RVSP was also linked to PEEP, ALT, and the partial pressure of inspired oxygen to oxygen (PaO_2/FiO_2) ratio. D-dimer, CRP, and hs-TnI did not connect with it [17].

RV abnormalities were identified in 185 of the 1216 Covid-19 patients examined by Bleakley et al. [17]. In contrast to these findings, there was no correlation found between the occurrence of RV dysfunction and biomarker increase (troponin or natriuretic peptides). The study did not identify the precise patterns of RV impairment or the criteria that were employed to assess RV function. On the other hand, prior findings from single center investigations with Covid-19 populations that are not essential consistently reveal a loss in RV longitudinal function as opposed to radial function.

Even when protective or noninvasive breathing techniques are employed, echocardiographic surveillance is crucial for these patients throughout their clinical course because to the influence of right ventricle dysfunction on Covid-19 mortality **[18]**.

RV impairment's substantial impact was consequently not detected by TAPSE or RVS measurements of long-axis function. As a compensatory measure for radial dysfunction, these values were actually often hyperdynamic **[17]**.

The accuracy of RV function evaluation may have been compromised by the difficulty of RV echocardiographic imaging in Covid-19 patients, particularly when mechanical ventilation is in place. Nonetheless, RV dysfunction is not indicative of poorer outcomes in this context and is comparable to that observed in patients with non-Covid-19 ARDS in patients with Covid-19-related critical illness **[14]**.

RV dilatation can lower the pressure gradient for the subendocardial coronary blood flow with a concomitant decrease in right ventricular contractility when it elevates the right ventricular distending pressure in response to an increase in afterload **[19]**.

Although the study findings, it has some limitations. First off, Covid-19 had been verified in every patient in this trial. Since no control data from non-Covid studies were available, it is not feasible to directly compare our findings with patient groups with RV issues in other investigations. Second, the sample size is still rather small and susceptible to the intrinsic constraints of smaller cohorts, even if it is greater than many prior research. Thirdly, it is advised that future research validate the relationships we have shown in cohorts that are comparable to our own.

Conclusion

RV dysfunction increases in COVID-19 patients with respiratory symptoms as their clinical severity increases. Various echocardiographic techniques were used to identify RV dysfunction; nevertheless, RV FAC, the most accurate technique, identified RV dysfunction in 29% of patients. The CT severity score and RV MPI have a substantial positive association; whereas, the CT severity score, RV FAC, TAPSE, and TASV have a significant negative correlation.

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Conflicts of interest
There are no conflicts of interest.

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