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Assessment of Right Ventricular Function by Three-Dimensional Echocardiography in Healthcare Workers Recovered from COVID-19 Infection

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ABSTRACT

Background: Individuals diagnosed with COVID-19 and pre-existing heart disease have more grave outcomes. The potential prognostic value of right ventricular dysfunction (RVD) in patients with COVID-19 remains uncertain, as existing studies are limited in size and scope. The RV functions could be evaluated more accurately by 3D echocardiography. The 3D-Echo-derived RVEF is a prognostic indicator for cardiovascular events among individuals with preexisting cardiovascular diseases.

Objectives: This study aimed to assess the RV function and size in healthcare workers recovered from COVID-19 infection by 3D echocardiography.

Methods: The study included 50 healthcare professionals at Ain Shams University Hospitals who had recovered a PCR-positive COVID-19 infection with a mild or moderate clinical presentation. All study patients were examined by 2D & 3D echocardiography.

Results: Fifty patients were included, and 32 were affected (64.0%) as measured by RVEF. The mean duration since infection was 11 months compared to 16 months in normal patients, which was statistically significant with a P value ≤ 0.001. Of the 32 affected patients, 17 had chest pain (53.1%) while 4 patients only had chest pain with infection and RV function was normal by 3D Echo (22% of normal patients) and this is statistically significant with the P value 0.034. Out of 18 normal patients, 12 patients had a fever (66.7%) while 11 had a fever out of 32 affected patients (34.4%), which was statistically significant with a P value of 0.02.

Conclusion: 3D echo effectively assesses RV function and detects subclinical impairment in healthcare workers post-COVID-19 recovery.

Keywords: Post-COVID, Healthcare, 3D Echocardiography.

INTRODUCTION

The year 2020 witnessed a substantial global impact due to the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated illness, commonly referred to as coronavirus disease 2019 (COVID-19). Earlier in the same year, the World Health Organization officially declared the situation to be a pandemic [(1)]. As of July 13th, 2021, the global death toll attributed to COVID-19 has exceeded 4 million [(2)]. Consequently, this has had profound consequences on healthcare systems, societal dynamics, and economic conditions.

The primary cause of the disease's high mortality and severity is respiratory complications, particularly the occurrence of severe pneumonia that progresses to acute respiratory distress syndrome (ARDS). Furthermore, it seems that individuals with this condition experience an impact on lung microcirculation in addition to the direct involvement of the alveoli. The results obtained from postmortem examinations reveal the existence of pulmonary endothelial dysfunction, which is characterized by an increased inflammatory infiltration and the formation of microvascular thrombosis [(3)].

The disorders mentioned above possess the capacity to lead to increased pulmonary pressures and an excessive burden on the right ventricle. Nevertheless, cardiovascular issues have been recognized as a predominant concern among these individuals. Several factors can influence the severity and clinical progression of the disease. Nevertheless, there is a consistent body of evidence indicating that individuals afflicted with COVID-19 may experience a notable deterioration in their health due to the presence of cardiovascular ailments, including arrhythmias, myocardial dysfunction, and myocardial damage [(4,5,6)].

The combination of lung parenchymal involvement, pulmonary microvascular pathologic alterations, right ventricular pressure overload, and direct myocardial injury collectively contributes to a deleterious impact on the function of the right ventricle. The potential association between right ventricular dysfunction (RVD) and worse outcomes in individuals with COVID-19 has been explored in limited exploratory investigations. However, the prevalence of RVD and its relationship with outcomes in COVID-19 patients remain unclear. Examining the frequency of right ventricular dysfunction (RVD) and its corresponding consequences in individuals diagnosed with COVID-19 could facilitate the adoption of customized approaches in the identification, prevention, and management of right ventricular impairment [(7)]. However, till now, little is known about the cardiac manifestations of COVID-19 because all the data gathered until now were based on laboratory and clinical evaluations or case reports in deteriorating patients.

We need more follow-up research on the patients who recovered from their illness to assess the short- and long-term clinical implications of cardiac disease in COVID-19 and to assess the pathogenesis of RV dysfunction in this disease [(8)]. Visual examination is the

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most commonly used method to quantify right ventricular function (RVF). There exist numerous potential pitfalls that may result in the overestimation or underestimation of function. When employed as a sole parameter, visual examination is an imprecise technique for assessing RVF [9, 10]. Consequently, guidelines recommend incorporating at least one additional parameter to quantify RVF.

Numerous echocardiographic parameters for right ventricular failure (RVF) have been established and subsequently validated. Each of the parameters possesses notable limitations and potential drawbacks. The parameter most frequently employed for quantifying right ventricular function (RVF) is TAPSE. The M-mode technique is utilized to measure the maximum systolic excursion of the lateral tricuspid annulus in an apical 4-chamber view. The Tricuspid Annular Plane Systolic Excursion (TAPSE) relies on a unidimensional assessment, thus offering only a limited representation of the overall right ventricular (RV) function. A TAPSE of < 17 mm indicates RV dysfunction [11].

Tissue Doppler imaging is utilized to measure the longitudinal velocity of the tricuspid annular plane from the base to the apex, specifically focusing on the free lateral wall (S'). Since the method is angle-dependent, the Doppler beam has to be aligned parallel to the motion of the free lateral wall towards the apex. The measurement is reproducible and easily obtained. A comparison with MRI-derived RV ejection fraction (RVEF) showed a significant correlation with S’ [12].

An S’ value of 0.095 m/s indicates RV dysfunction. The fractional area change (FAC) is a 2D surrogate for RVEF. It is performed by tracing the endocardial RV borders during diastole and systole and is calculated by the following formula: 100 × (RV-Area end-diastolic [ED] − RV-Area end-systolic [ES]) / RV-Area ED. A RV-focused 4-chamber view is essential to ensure the entire endocardial border to be visible in end-systole and end-diastole. Trabeculations and the tricuspid valve leaflets are included when tracing the area. A value of less than 35% indicates RV systolic dysfunction. So far, the problem for echocardiographers has been the unreliable estimation of RVEF via 2D echocardiography since it is not able to calculate true volumes. This limitation is overcome with 3D echocardiography, which does not rely on geometric assumptions but calculates true 3D volumes. The RVEF derived by 3D echocardiography was an independent predictor of adverse cardiovascular outcomes in patients with various cardiovascular diseases [11].

However, the 3D method requires special transducers, dedicated hardware, and software, and is associated with a higher cost and additional time to perform the measurements. In addition, good image quality is mandatory for correct analysis. The future will show to what degree 3D echocardiography will be implemented into daily clinical practice when evaluating RVF. Thus we aimed to assess right ventricular functions and dimensions using 3D echocardiography in healthcare workers recovered from COVID-19 infection.

PATIENTS AND METHODS

Study design:

Our study is a pilot cross-sectional observational study that was conducted in Ain Shams University Hospitals on 50 adult healthcare workers who recovered from proven (+VE PCR) COVID-19 infection 4-8 weeks before the study. All the included healthcare workers had either a history of mild or moderate COVID-19 infection.

Mild Illness: Individuals who had any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who did not have shortness of breath, dyspnea, or abnormal chest imaging.

Moderate Illness: Individuals who showed evidence of lower respiratory disease during clinical assessment or imaging and who had an oxygen saturation (SpO_2) ≥ 94% on room air at sea level [8].

Ethical Considerations: The research protocol was in accordance with the declaration of Helsinki. Approval was obtained from The Ethical Committee at Ain Shams University. All participants gave informed written consents with consideration of adequate privacy and confidentiality.

Inclusion criteria: All stable healthcare workers recovered from COVID-19 (symptoms-free and - ve PCR) at least 4-8 weeks before the study. All the included healthcare workers had documented mild to moderate COVID-19 infection. Neither age nor sex predilection will be done. Willing and capable of providing informed consent.

Exclusion criteria: Patients with rheumatic heart disease. Patients with congenital heart disease. Patients with documented pulmonary embolism before COVID Infection. Patients with significant (more than grade II) valvular lesions. Patients with ischemic heart disease. Patients with documented pulmonary disease.

Study Tools: All patients after writing informed consents were subjected to the following at baseline:

History taking: Full history taking with recording of age, gender, co-morbidities (the presence of, diabetes mellitus, hypertension & smoking), and medications.

Full clinical assessment of the presenting patients including Complexion – Decubitus. Arterial blood pressure. - Heart rate. Respiratory rate. - Oxygen saturation. Chest auscultation. - Cardiac auscultation.

12 lead surface ECG done during admission with active COVID-19: All healthcare workers underwent an ECG recording with detailed analysis of ST-segment deviations and T-wave abnormalities at baseline.

Standard transthoracic 2D echocardiographic examination:

These measurements were taken: FAC: Apical 4 chambers and RV focused view assessed RV fractional area change. The RV FAC is calculated: Fractional area change = RV end-diastolic – end-systolic / RV end-diastolic. In apical 4 chamber view, tricuspid annulus peak systolic (S') velocity. In the apical 4-chamber view, M-Mode measures tricuspid annular plane systolic excursion (TAPSE).

Real-time 3D echocardiography: 3D echocardiography was performed with a dedicated wide-angle, broadband 4V (Vivid E95) matrix-array transducer. Before acquisitions, pictures were adjusted for endocardial boundary imaging, altering overall gain, time gain, and compression. They were then digitally stored for offline analysis by 4D Auto RVQ, Echo Pac software v202, yielding the following parameters: BSA indices 3D RV end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction (EF), and stroke volume (SV).

Statistical Analysis

SPSS version 29 was utilized. The numerical variables were represented as mean ± standard deviation (SD). T-Test calculation for 2 independent means in normal distribution. Statistical significance was defined at $p \leq 0.05$, with a highly significant threshold of ≤ 0.001.

RESULTS

The patients' demographics, COVID diagnosis details and 2D echocardiographic data are represented in tables (1), (2) and (3) respectively.

Figure (1) shows the prevalence of each of the symptoms of the COVID infection within the studied population.

The details of the 3D echocardiographic studies performed are represented in table (4).

Table (1): Demographic Data of the studied patients

Personal History		**Total no. = 50**
Age	Mean ± SD	28.36 ± 6.22
	Range	23 – 50
Occupation	Doctor	27 (54.0%)
	Nurse	23 (46.0%)
Gender	Female	6 (12.0%)
	Male	44 (88.0%)
Smoking	No	35 (70.0%)
	Yes	15 (30.0%)
DM	No	50 (100.0%)
	Yes	0 (0.0%)
HTN	No	49 (98.0%)
	Yes	1 (2.0%)

Table (2): COVID diagnosis details among the studied patients

COVID Diagnosis		**Total no. = 50**
Duration (months)	Mean ± SD	13.20 ± 4.27
	Range	7 – 21
Method	PCR	50 (100.0%)

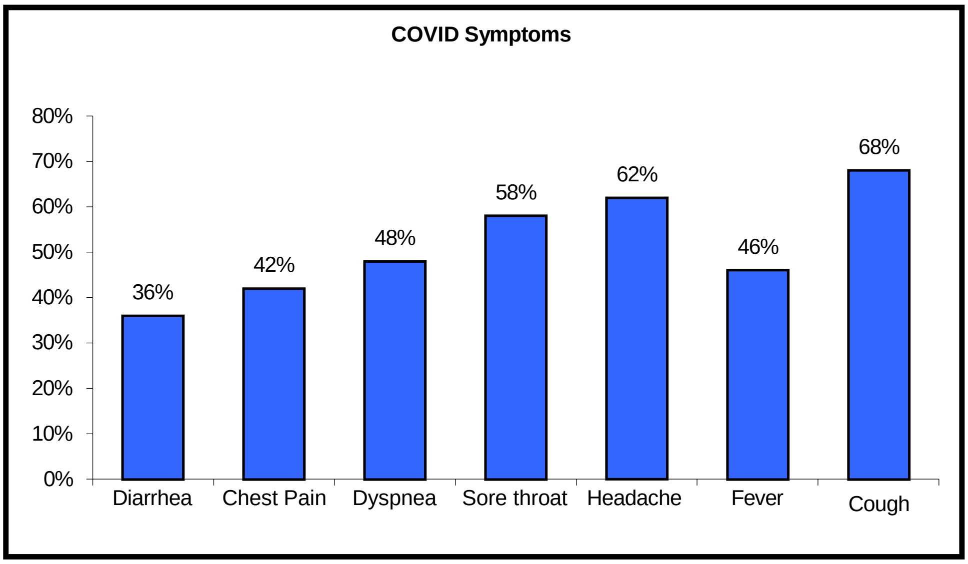

Figure (1): COVID symptoms among the studied patients

Table (3): 2D ECHO details among the studied patients

2D ECHO		**Total no. = 50**
RV FAC	Mean ± SD Range	37.66 ± 7.92 17 – 54
	Normal (>= 35) Affected (<35)	39 (78.0%) 11 (22.0%)
TAPSE	Mean ± SD Range	23.96 ± 4.33 16 – 35
	Normal (>= 17) Affected (<17)	42 (84%) 8 (16%)
RV S'	Mean ± SD Range	14.14 ± 2.70 8 – 22
	Normal (>= 9.5) Affected (<9.5)	40 (80%) 10 (20%)

Table (4): 3D ECHO details among the studied patients

3D ECHO		**Total no. = 50**
RVEDVI	Median (IQR) Range	58.55 (35.33 – 72.98) 19.97 – 144.28
RVESVI	Median (IQR) Range	34.56 (22.71 – 39.42) 11.48 – 79.78
RV EF	Mean ± SD Range	42.52 ± 6.33 27 – 55.8
	Normal (>= 45) Affected (< 45)	18 (36.0%) 32 (64.0%)
RVSVI	Median (IQR) Range	24.9 (15.71 – 30.69) 8.49 – 64.5

Table (5) and figure (2) showed that there was no statistically significant relation between RV impairment and mean age, gender, smoking, and HTN while there was a statistically highly significant relation between RV impairment and occupation with more percentage of nurses were found in affected cases with p-value < 0.001

Table (5): Relation between RV EF impairment and personal history of the studied patients

Personal History		**RV EF**		**Test value**	**P-value**	**Sig.**
		Normal (>= 45)	**Affected (< 45)**			
		No. = 18	**No. = 32**			
Age	Mean ± SD Range	26.94 ± 1.73 23 – 30	29.16 ± 7.60 23 – 50	-1.212•	0.231	NS
Occupation	Doctor Nurse	16 (88.9%) 2 (11.1%)	11 (34.4%) 21 (65.6%)	13.782*	0.000	**HS**
Gender	Female Male	0 (0.0%) 18 (100.0%)	6 (18.8%) 26 (81.2%)	3.835*	0.050	NS
Smoking	No Yes	15 (83.3%) 3 (16.7%)	20 (62.5%) 12 (37.5%)	2.381*	0.123	NS
DM	No Yes	18 (100.0%) 0 (0.0%)	32 (100.0%) 0 (0.0%)	–	–	–
HTN	No Yes	18 (100.0%) 0 (0.0%)	31 (96.9%) 1 (3.1%)	0.574*	0.449	NS

P-value > 0.05: Non-significant P-value < 0.05: Significant, P-value < 0.01: Highly significant *:Chi-square test; •: Independent t-test

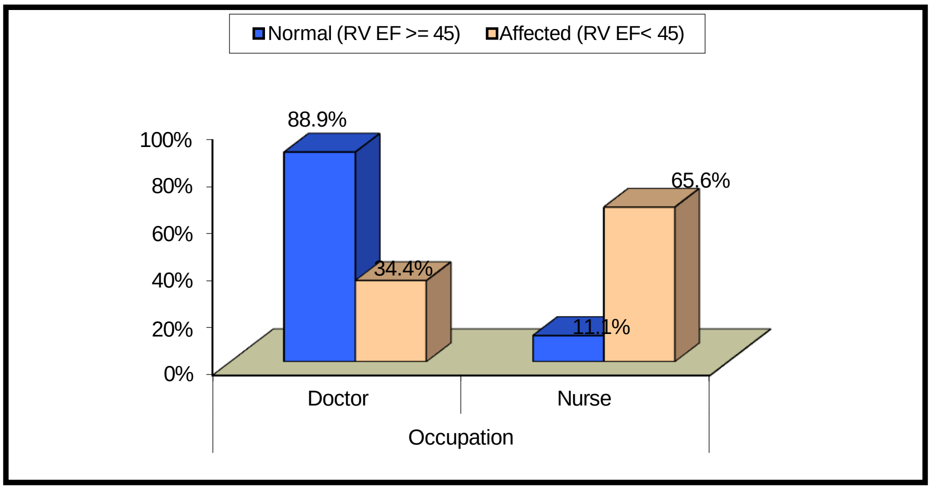

Figure (2): Relation between RV EF impairment and occupation.

Table (6) showed that there was a statistically highly significant relation between RV impairment and duration from COVID-19 infection with a p-value < 0.001. As regards symptoms, it was noted that there was a statistically significant relation between chest pain and RV impairment with a P-value of 0.034. Also, between fever and RV impairment with a P-value of 0.028. 65.6% of RV-affected patients had no fever during infection. However, there was no statistically significant relation between RV impairment and other symptoms such as diarrhea, sore throat, headache, and cough.

Table (6): Relation between RV EF impairment and COVID diagnosis details

COVID Diagnosis		RV EF		Test value	P-value	Sig.
		Normal (>= 45)	Affected (< 45)			
		No. = 18	No. = 32			
Duration (months)	Mean ± SD	16.67 ± 2.95	11.25 ± 3.62	5.412•	0.000	HS
	Range	12 – 21	7 – 20			
COVID Symptoms	Diarrhea	7 (38.9%)	11 (34.4%)	0.102*	0.750	NS
	Chest Pain	4 (22.2%)	17 (53.1%)	4.516*	0.034	S
	Dyspnea	7 (38.9%)	17 (53.1%)	0.935*	0.333	NS
	Sore throat	11 (61.1%)	18 (56.2%)	0.112*	0.738	NS
	Headache	10 (55.6%)	21 (65.6%)	0.496*	0.481	NS
	Fever	12 (66.7%)	11 (34.4%)	4.836*	0.028	S
	Cough	13 (72.2%)	21 (65.6%)	0.230*	0.631	NS

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test; •: Independent t-test.

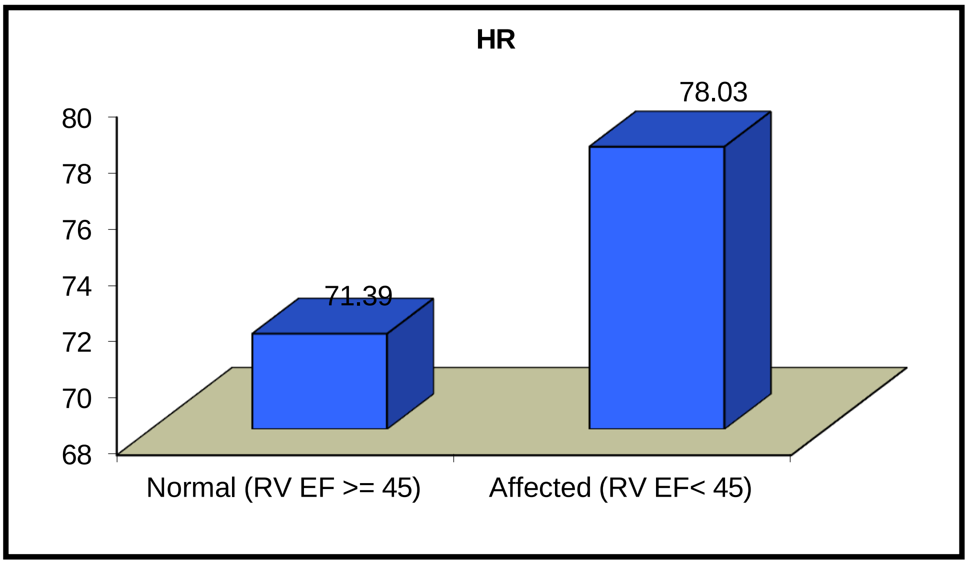

Figure (3): Relation between RV EF impairment and mean heart rate (HR)

Table (7) showed that the sensitivity of the RV FAC to detect RV impairment was 34.4% while the specificity was 100%. It also showed that the accuracy of the RV FAV was 0.58.

Table (7): ROC curve for 2D ECHO to detect cases with RV impairment.

	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
RV FAC	11	18	0	21	34.40%	100.00%	100%	46.2%	0.580

The previous univariate logistic regression analysis showed that all the previous variables were associated with RV impairment. The multivariate logistic regression analysis showed that occupation (nurse), duration ≤ 13 months, and HR >74/min were the most associated risk factors with RV impairment (Table 8).

Table (8): Univariate and Multivariate logistic regression analysis for factors associated with RV impairment.

	Univariate				Multivariate (Backward: Wald)			
	P-value	Odds ratio (OR)	95% C.I. for OR		P-value	Odds ratio (OR)	95% C.I. for OR	
			Lower	Upper			Lower	Upper
Nurse	**0.001**	15.273	2.960	78.814	**0.029**	11.117	1.274	97.023
Duration ≤ 13 months	**0.000**	28.571	5.261	155.170	**0.006**	15.915	2.241	113.049
Chest Pain	**0.039**	3.967	1.070	14.705	–	–	–	–
Fever	**0.032**	0.262	0.077	0.889	–	–	–	–
HR >74	**0.011**	1.148	1.032	1.277	**0.033**	8.120	1.185	55.638

DISCUSSION

According to the findings of our study, RV systolic function as assessed by FAC was normal in 39 patients (78%) and impaired in 11 patients (22%). TAPSE was normal in 42 patients (84.0%), while it was abnormal in 8 patients (16.0%). While maximal systolic velocity (S') was normal in 40 patients (80%) and it was abnormal in 10 patients (20%). RVEF determined that there were 32 affected patients (64%) and 18 normal patients (36%) among the 50 patients studied. Similar to the findings, **Yanting *et al.*** [(13)]who investigated the prognostic value of right ventricular ejection fraction assessed by 3D echocardiography in COVID-19 Patients, 2D-RVFWLS and 3D-RVEF were significantly reduced in COVID-19 patients compared to controls (27.2% & 4.4% vs. 22.9% & 4.8%, P 0.001). Critical patients were more likely than general and severe patients to have a higher incidence of acute cardiac injury and acute respiratory distress syndrome (ARDS), as well as a poorer prognosis. The participants of that research included 128 COVID-19 patients and 31 healthy controls. COVID-19 severity of illness was used to divide patients into three subgroups (general, severe, and critical). The acquisition of conventional RV structure and function parameters, RV free wall longitudinal strain (FWLS), and 3D-RVEF. RVFWLS was measured using speckle tracking echocardiography in two dimensions. 3DE has acquired RVEF.

Comparatively, our study was conducted on post-COVID healthcare workers to detect subclinical RV impairment in mild and moderate infection, and it was discovered that 64% of patients with 3D Echo had RV impairment, whereas 22% of patients with 2D Echo were affected. Evidently, the 3D Echo was superior for assessing RV function and detecting subclinical impairment. Of the 32 patients affected by 3D Echo, 21 nurses (65.6%) and 11 physicians (34.4%) were infected, which was statistically highly significant due to the high exposure of nurses to COVID-19 patients and viral load. This was the first study to use 3D echocardiography to examine RV impairment in post-COVID healthcare workers. The average heart rate of patients with RV impairment was 78 beats per minute, compared to 71 beats per minute for patients with normal RV function. This difference was statistically highly significant, leading to the conclusion that COVID-19 patients with heart rates above 74 are more likely to develop RV impairment in the future.

Of the 50 patients studied, 44 were male and 6 were female. All six females had impaired RV function, while 26 males were impaired and 18 had normal RV function. This was statistically insignificant because there were so few females in the study. 15 of the fifty patients studied were smokers. There were 12 smokers (37.5%) among the 32 affected patients and 20 non-smokers (62.5%). There were 15 non-smokers (83.5%) and 3 smokers (16.5%) among the 18 normal RV patients, and this difference was not statistically significant.

CONCLUSION

It was found that post-COVID healthcare workers had significantly impaired RV function. It was demonstrated that 3D Echocardiography is more sensitive than 2D Echocardiography at detecting subclinical RV impairment. It was also discovered that nurses were more susceptible to RV impairment after contracting COVID than physicians, which may be a result of their greater exposure to COVID-19 patients and viral load. 3D Echocardiography may be utilized for both the detection and follow-up of possible long-term right ventricular dysfunction following COVID-19 disease of mild and moderate severity.

- **Conflicts of Interest:** None of the authors have a conflict of interest to declare.
- **Funding resources:** No funding was received from any institution.

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