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Assessment of The Right Ventricle Using Speckle-Tracking and Global Longitudinal Strain in Patients Recovered From COVID-19 Infection

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ABSTRACT

Background: COVID-19, triggered by the SARS-CoV-2 virus, was shown to have a profound effect on cardiac function. However, the long-term implications of myocardial damage in individuals who have recovered from the infection are not yet fully understood.

Aim: This study aimed to identify the early changes in right ventricular (RV) function three months after recovery from COVID-19 using Speckle Tracking Echocardiography (STE) and Global Longitudinal Strain (GLS).

Methods: This study was designed as a cross-sectional descriptive analysis and included 104 patients who had recovered from COVID-19 pneumonia during a three-month timeframe. The participants have been categorized into two groups based on the severity of their illness: mild cases and moderate/severe cases.

Results: The demographic characteristics of the two groups broadly were similar with no statistically significant differences. The average age of the participants was 48.8 ± 10.7 years, with males representing 55.8% of the study population. The average body mass index (BMI) was 23.6 ± 0.71 kg/m^2. Furthermore, 45% of the participants had diabetes, and 34% were diagnosed with hypertension. Significant statistical differences were observed in right ventricular function parameters between the moderate/severe group and the mild group. The moderate/severe group showed a marked early reduction in both RV-GLS and RV-FWLS compared to the mild group. However, no early impairment was detected in right ventricular longitudinal function as measured by TAPSE.

Conclusion: Speckle-tracking echocardiography proved to be a valuable tool for early detection of abnormalities that are not easily identified by conventional echocardiography, particularly in assessing strain on the right ventricle.

Keywords: COVID-19, RV-GLS, RV-FWLS, Echocardiogram.

INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has rapidly diffused to more than 170 different countries, resulting in significant illness and death. Research has indicated that COVID-19 has the potential to inflict harm on the heart and is associated with elevated mortality rates in individuals [1, 2].

Myocardial damage associated with COVID-19 might occur suddenly and persist during the recovery phase and possibly beyond. However, we still have limited knowledge about how long this heart damage persists in recovered COVID-19 patients [3].

Elevated RV afterload has been observed to render the right ventricular (RV) function more susceptible to deterioration. Echocardiography is the predominant technique employed in clinical settings to assess the morphology and performance of the RV. Nevertheless, traditional echocardiographic criteria have poor diagnostic efficacy and may be inadequate in identifying initial abnormalities in right ventricular systolic function [2]. Speckle-tracking echocardiography (STE) represents a sophisticated method that accurately and dependably assesses cardiac activity. It can identify subtle changes in cardiac function that may not be clinically apparent. Moreover, research has demonstrated that RV longitudinal strain (RVLS) assessed by 2D speckle tracking echocardiography (STE) has been established as a significant diagnostic indicator, hence confirming its importance in this particular patient population. This is particularly significant because the majority of patients have intact traditional echocardiographic characteristics, which makes it challenging to detect and assess the risk [4,5].

The study aimed to detect early abnormalities in RV function three months after recovery from a coronavirus infection. This is achieved by assessing the right ventricle using STE and GLS Echocardiography inpatients admitted to Suez Canal University Hospital (SCUH).

MATERIALS AND METHODS

104 adult patients were included in the study. All patients (18 years of age or older) were diagnosed with COVID-19 pneumonia, confirmed through PCR testing. After a 3-months recovery period, the patient was sent from the chest and cardiology clinic to the non-invasive cardiology unit at Suez Canal University Hospital (SCUH) to undergo transthoracic echo (TTE) between March 22 and September 17, 2023.

Patients who got SARS-CoV-2 may exhibit a diverse array of clinical symptoms, which can vary from having no symptoms at all to experiencing severe sickness. Typically, adults who became ill with SARS-

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CoV-2 can be categorized into different levels of sickness severity:

• **Mild illness**: Patients presented with any COVID-19 symptoms, for example cough, fever, headache, sore throat, fatigue, nausea, diarrhea, vomiting, muscle pain, or loss of smell or taste, but without breathing difficulties or abnormal chest imaging and do not require hospitalization.

• **Moderate illness**: Patients who exhibited clinical signs of lower respiratory tract disease, as confirmed through evaluation or imaging, yet maintain an oxygen saturation (SpO_2) level of 94% or above while breathing ambient air at sea level, fall within this category.

• **Severe illness**: This condition is characterized by several critical criteria: Blood oxygen saturation (SpO_2) of less than 94% while breathing ambient air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) of less than 300 mm Hg, a respiratory rate of more than 30 breaths per minute, or the presence of lung infiltrates covering more than 50% of the lung fields. Patients who meet any of these criteria are considered to be in a critical condition and require immediate hospitalization for intensive medical intervention.

The study participants were categorized into two distinct groups according to their clinical presentation history: mild and moderate/severe cases, with critically ill and mechanically ventilated patients excluded from the study.

To collect essential clinical data from each patient, a standardized questionnaire was employed. Additionally, all participants in the study underwent thorough examinations, which included both general assessments and detailed evaluations of cardiac function at localized levels. Twelve lead ECG at rest and echocardiography were done to all patients. Echocardiography was conducted using a Vivid iq system from General Electric Healthcare, equipped with a 2.5-MHz phased array probe. Each chamber's function and size, valvular lesions, and the possible presence of pulmonary hypertension have been assessed.

A retrospective analysis of the measurements was conducted using archived images in an offline manner. This analysis was carried out independently by two observers, who had no access to the clinical data to ensure impartiality and accuracy of the results.

To assess the right ventricle, the basal diameter was measured from the apical four-chamber view during the end-diastole (ED) phase. The RV wall thickness was evaluated using the subcostal view, particularly in the emergency department (ED). The tricuspid annular plane systolic excursion (TAPSE) was determined using M-mode at the lateral tricuspid annulus. The change in fractional area (FAC) of the RV was calculated by tracing the endocardial borders during both the end-diastole (ED) and end-systole (ES) phases. The right ventricle was considered dilated if the basal diameter exceeded 41 mm. Systolic dysfunction of the RV was identified by a fractional area change below 35% or a tricuspid annular plane systolic excursion of less than 17 mm [6, 7].

Doppler Echocardiography: Following this, PW Doppler was utilized to both the tricuspid valve (TV) and the pulmonary valve from the apical four-chamber view to obtain consistent results and accurately measure the peak velocity of the pulmonary valve. These measurements were taken during a phase of quiet breathing, specifically at the end of expiration. To further assess the right ventricle, a continuous-wave (CW) Doppler was employed on the tricuspid valve to determine the systolic pressure in the right ventricle (RVSP). The calculation considered the expected pressure in the right atrium, taking into account the size and collapsibility of the inferior vena cava (IVC) and making necessary changes [8, 9].

Strain analysis: Strain analysis was performed using the speckle-tracking approach. An experienced cardiologist determined the strain, using the technique outlined in earlier studies [10,11], and the results were presented as an absolute numerical value. The RV longitudinal strain was analyzed using an RV-focused image acquired through the apical four-chamber views [12]. Once the RV endocardial border has been defined, an automated process generated the region of interest. Manual adjustments were carefully performed to ensure precise alignment with the myocardial wall's thickness within the RV. The interventricular septum and the free wall of the right ventricle were automatically divided into three distinct segments: basal, mid, and apical regions. The global longitudinal strain of the right ventricle (RV-GLS) was calculated by averaging the measurements obtained from all six segments. Similarly, the longitudinal strain of the right ventricle's free wall (RV-FWLS) was calculated by taking the average of the values acquired from the three segmented regions of the free wall, as depicted in Figure 1 [13].

Ethical consideration: The research protocol was approved by the Ethics Committee of Faculty of Medicine, Suez Canal University. Participants in the study gave their agreement after being fully informed with a comprehensive explanation of the study's objectives, methodologies, and potential implications. Written informed consents were obtained from all participants. The research was conducted in full conformity with the ethical principles established by the World Medical Association guidelines outlined in

the Declaration of Helsinki, which offers comprehensive direction for conducting investigations involving human participants.

Statistical analysis

The data were initially collected and structured using Microsoft Excel, and subsequently underwent an extensive statistical analysis utilizing the Statistical Package for the Social Sciences (SPSS), version 27.0. Statistical significance tests were performed, using a probability value (P value) of ≤ 0.05 as statistically significant, guaranteeing a 95% confidence level. Descriptive statistics were presented as mean ± standard deviations for quantitative data, while qualitative data were expressed as percentages. For the comparison of qualitative factors, the Fisher's exact test or Chi-squared test was implemented, while unpaired t-tests was implemented to compare quantitative data between the two groups. The Pearson correlation coefficient was employed to evaluate the association between various parameters and GLS. Data pertaining to personal, clinical, and imaging were gathered, and the correlations between various parameters were established.

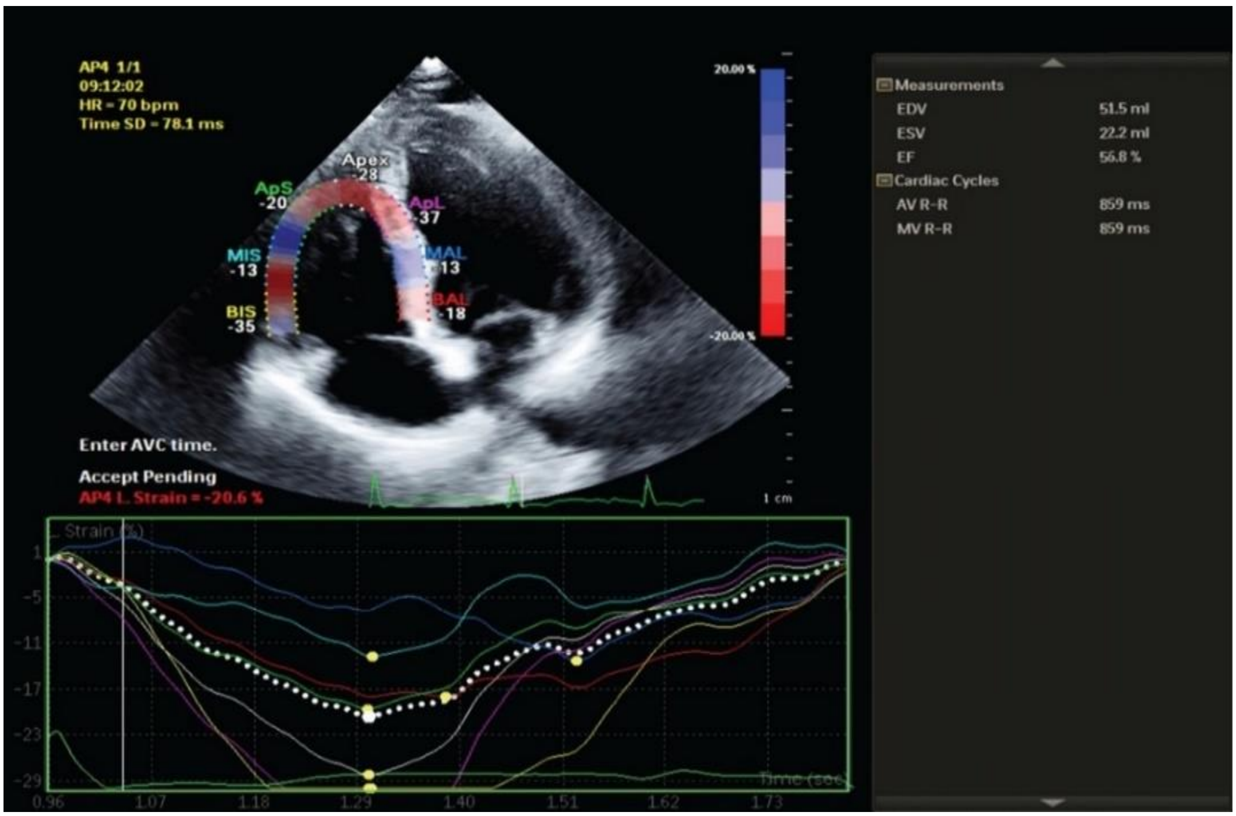

Figure (1): The assessment of longitudinal strain in the right ventricle was done using speckle tracking echocardiography (STE), which involved analyzing an image taken from the apical four-chamber view to obtain a detailed viewpoint [14].

RESULTS

A total of 104 patients, who were being monitored for SARS-CoV-2 pneumonia and met the precise criteria for inclusion were selected to be part of this study. Table (1) presented the fundamental demographic information, cardiovascular risk factors and clinical data. The average age was 48.8 ± 10.7 years, with the majority being males (55.8%). The average BMI was 23.7 ± 0.71 kg/m^2. Additionally, 37.5% were diabetic and 44.2% were hypertensive. No noticeable differences were observed between the two groups in terms of gender, age, or cardiovascular risk factors, indicating that these demographic and health-related variables were comparable across both groups.

Table (1): Overview of the demographic data for all participants included in the study

		TOTAL (N=104)		Mild (N = 50)		Moderate/severe (N = 54)		P-value
		N	**%**	**N**	**%**	**N**	**%**	
Sex	**Male**	58	59.8%	27	54%	31	57.4%	**0.727 NS**
Age (years)	**Mean**	48.8		48.5		49.2		**0.739 NS**
	±SD	10.7		11.0		10.6		
BMI (Kg/m²)	**Mean**	23.7		23.6		23.8		**0.1 NS**
	±SD	0.71		0.82		0.59		
HTN		46	44.2%	22	44%	24	44.4%	**0.964 NS**
DM		39	37.5%	16	32%	23	42.6%	**0.265 NS**
Smoking		**48**	46.2%	24	48%	24	44.4%	**0.716 NS**

T: independent sample *t-test*. X2: Chi-square test. NS: p-value > 0.05 is considered non-significant

In Table (2), no statistically significant difference was found in CRP levels at the time of admission between the two groups under study. Nevertheless, there was a notable disparity in troponin levels, which was statistically significant (P-value of 0.035). These findings indicated that COVID-19 infection causes more significant damage to the heart than the inflammatory response itself.

Table (2): Comparison of laboratory data between mild and moderate to severe groups.

	MILD n=50	Moderate to severe n=54	p-value
CRP (mg/L)	**9.5±8.3**	**19.8±12.8**	**0.524**
Troponin (ng/ml)	**5.1±3.9**	**53.3±19.4**	**0.032***

NS: p-value > 0.05 is considered non-significant.

In Table (3), comparing the echo data between the studied groups. The comparison indicated that there was no significant difference among the mild and moderate/severe groups in terms of RV basal diameter, TAPSE, RV mid diameter, and RV FAC. This suggests that the initial myocardial changes caused by viral infection do not impact the standard echocardiographic measurements of RV. However, notable differences were observed in the RV GLS and the right ventricular free wall longitudinal strain (RV FWLS) when comparing the moderate/severe group to the mild group (P-values of 0.014 and 0.002 respectively). This suggests that 2D-strain echocardiography can clarify early affection of the right ventricle that was not evident through basic 2D measurements. Additionally, the tested groups exhibited notable disparities in tricuspid valve velocity and pulmonary artery systolic pressure (PASP) (P-values of 0.014 and 0.036 respectively). This suggests that pulmonary hypertension is frequently the result of COVID-19 infection.

Table (3): Summary of analyzed ECHO data in all subjects under investigation

		TOTAL (N=104)	Mild (N = 50)	Moderate/severe (N = 54)	T	P-value
TAPSE	**Mean ±SD**	**2.23 0.25**	**2.28 0.13**	**2.22 0.31**	**1.3**	**0.193 NS**
RV FAC	**Me-an ±SD**	**39.1 6.02**	**42.2 3.1**	**39.7 4.1**	**3.4**	**0.081 NS**
RV GLS	**Mean ±SD**	**18.3 3.46**	**19.2 3.92**	**17.5 2.77**	**2.5**	**0.014 S**
RV basal	**Mean ±SD**	**3.45 0.35**	**3.19 0.13**	**3.30 0.31**	**2.3**	**0.21 NS**
RV MID	**Mean ±SD**	**2.60 0.36**	**2.43 0.33**	**2.6 0.38**	**2.44**	**0.16 NS**
RVFWLS	**Mean ±SD**	**20.4 3.79**	**21.0 3.93**	**18.7 3.4**	**3.1**	**0.002 S**
TV velocity	**Mean ±SD**	**3.2 0.30**	**2.97 0.15**	**3.08 0.27**	**2.4**	**0.014 S**
PASP	**Mean ±SD**	**39.8 6.58**	**35.5 3.64**	**37.6 6.3**	**2.1**	**0.036 S**

S: p-value < 0.05 is considered non-significant. HS: p-value < 0.001 is considered highly significant.
t: independent sample *t*-test. NS: p-value > 0.05 is considered non-significant

RV GLS was effective in distinguishing the moderate/severe group, with a cutoff value of less than -21. This cutoff achieved a sensitivity of 96.3%, a specificity of 32%, a positive predictive value (PPV) of 60.5%, and a negative predictive value (NPV) of 88.9%. The area under the curve (AUC) was calculated to be 0.62, with a p-value of 0.029. RVFWLS can distinguish the moderate/severe group with a cutoff level of less than 20.6, achieving 81.5% sensitivity, 56% specificity, 66.7% PPV, and 73.7% NPV. The AUC was 0.69 (p-value < 0.001) (Table 4 & figure 2).

Table (4): Evaluation of the diagnostic accuracy of right ventricular global longitudinal strain (RV GLS) in differentiating between the moderate and severe patient groups

	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	p-value
RV GLS	**< 21**	**0.62**	**96.3%**	**32%**	**60.5%**	**88.9%**	**0.029**
RVFWLS	**< 20.6**	**0.69**	**81.5%**	**56%**	**66.7%**	**73.7%**	**< 0.001**

PPV: positive predictive value. NPV: negative predictive value. AUC: Area under curve.

Utilizing the ROC curve analysis, it was demonstrated that:

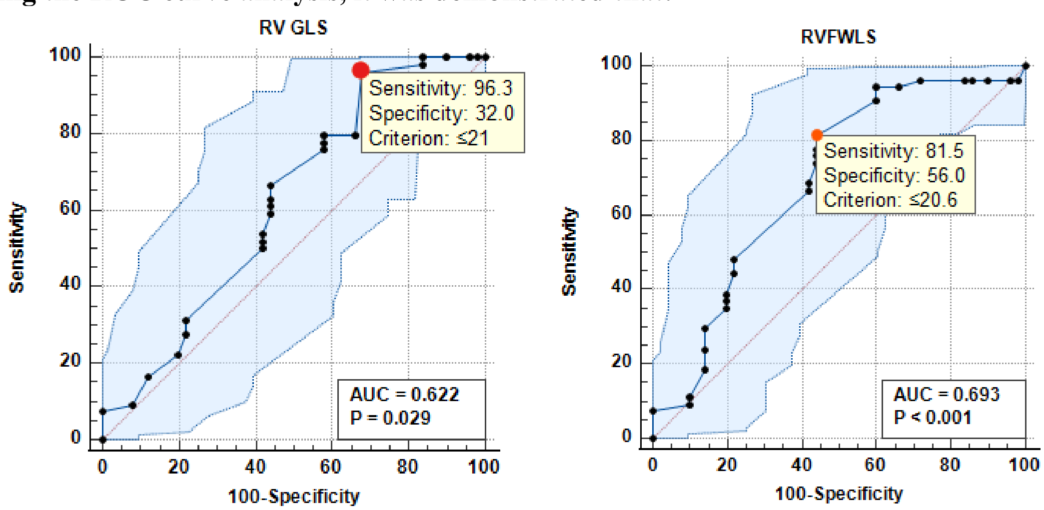

Figure (2): (ROC) curve was generated to compare the performance of (RV GLS) and (RVFWLS) in distinguishing between the mild group and the moderate/severe group.

DISCUSSION

The severity of RV dysfunction is important in predicting mortality in different patient groups. This is particularly important for developing ways to handle circulatory and respiratory difficulties in individuals with COVID-19 and lung conditions [(15)]. Our research investigated the early changes in RV function three months after recovery from COVID-19 by employing both RV-GLS and RV-FWLS measurements.

The study found a substantial decrease in both RV-GLS and RV-FWLS in the moderate/severe group compared to the mild group. This decline was observed even though standard TTE parameters for right ventricular dysfunction including TAPSE and RV-FAC, remained unchanged. The existing literature on COVID-19 presents a broad spectrum of evaluations regarding RV systolic function, with RV-FAC and TAPSE being the most frequently utilized parameters. RVFAC and TAPSE are important indicators of right ventricular function with RVFAC reflecting the overall systolic function of the TAPSE and RV indicating the longitudinal contraction of the RV. Numerous studies employ a variety of measurements to evaluate RV dysfunction, reporting a wide range of outcomes that are dependent on the severity of the disease within the sampled population [(16)].

A research indicated that TAPSE is significantly reduced in patients who exhibit wall motion abnormalities of the myocardium [(17)] and those who are critically ill [(18, 19)]. Thirty days following discharge from the hospital due to COVID-19, patients exhibited a marked decrease in TAPSE levels, particularly when compared to healthy individuals. This reduction is also apparent in patients who have unfortunately faced fatal outcomes [(20-25)]. A prospective case-control study demonstrated a significant reduction in TAPSE between COVID-19 patients compared to a healthy-matched control. The research further identified low TAPSE levels as independent risk factors contributing to COVID-related mortality [(26)].

Our research found no noticeable differences in TAPSE and RV-FAC measurements between the mild and moderate/severe groups. This finding suggests that in the early stages of the illness, TTE parameters used to indicate RV dysfunction may not serve as reliable predictors of mortality. This contrasts with previous studies that used different populations and different groups. It is possible that the standard parameters traditionally employed to evaluate RV performance may only capture a limited aspect of RV function, primarily focusing on the longitudinal contraction of the RV. These parameters could be affected by the angles at which the measurements are taken, potentially limiting their accuracy. Consequently, these standard parameters may not possess adequate sensitivity to detect subtle alterations in right ventricular (RV) function. Additionally, previous studies included critically ill patients and utilized different comparisons, such as comparing patients with healthy volunteers. RV strain, on the other hand, is not affected by angle, load, and passive tethering. This characteristic makes it a superior method for precisely evaluating both regional and global cardiac function, offering a more reliable and accurate indicator of myocardial contractility [(27)].

RV-GLS, as assessed by a two-dimensional speckle tracking echocardiography (2D-STE), is recognized as a highly effective and precise technique for evaluating right ventricular systolic function. Its accuracy has been validated through comparisons with RVEF measurements obtained via cardiac magnetic resonance (CMR) in various clinical scenarios, including conditions such as heart failure, pulmonary hypertension (PH), myocardial infarction, pulmonary embolism, valvular heart diseases and cardiomyopathies [(28–31)]. Two-dimensional speckle tracking technology enables precise monitoring of cardiac tissue motion by examining numerous pixels in a particular area of interest. It measures the relative change in myocardial length during diastole and systole. This change is measured by determining a ratio of a variance in myocardial length between the end of systole and the end of diastole. The implementation of two-dimensional speckle tracking technology facilitates a comprehensive evaluation of right ventricular dysfunction. This method is not affected by the angle of measurement and provides reliable results that can be reproduced accurately. This possesses advantageous practical worth [(27)]. A meta-analysis indicated that the normal range for RVLS is -27 ± 2% [(32)]. However, it appears that an RVLS cutoff of -20% to -21% is capable of identifying abnormal RV function [(33)].

Our study demonstrated that an RV-GLS value of -21% serves as a critical cutoff point for detecting RV dysfunction, achieving a specificity of 32% and a sensitivity of 96.3%. The research conducted by **Li *et al.*** [(2)] has shown which RV-GLS can serve as a reliable indicator of death in patients with COVID-19, regardless of other clinical factors. The study established that a threshold of -23% for RV-GLS demonstrated a high degree of accuracy in predicting patient outcomes. This was reflected by an area under the curve (AUC) of 0.87, a p-value less than 0.001, a specificity of 64.7%, and an impressive sensitivity of 94.4%. **Baycan *et al.*** [(15)] discovered that people in the severe group had significantly lower RV-GLS values than those in the control group or non-severe. The RV-GLS measurements were -17.2 ± 2.3, -20.5 ± 3.2, and -27.3 ± 3.1 respectively. The difference was statistically significant, with a P-value of less than 0.001 [(15)]. Additionally, **Hafez *et al.*** [(34)] reported a significant decrease in both RV-GLS (-15.1 ±

3.4 vs. -18.5 ± 3.2%, p < 0.001) and RV-FWLS (-17.2 ± 4.4 vs. -19.6 ± 5.2%, p < 0.001) in the mild group compared to the control group.

Study Limitation: Our study had various limitations that should be taken into account. The data were primarily obtained through a single facility that may restrict the applicability of the findings. In addition, the sample size was quite small, thereby compromising the reliability of the conclusions. Furthermore, there was an absence of sufficient 2D echocardiographic (2DE) data from patients prior to their COVID-19 infection, making it difficult to establish a comprehensive baseline for comparison. In addition, all echocardiography images were captured by a single operator as a safety measure to minimize the risk of infection, although these images were later reviewed and analyzed by two independent medical experts. Furthermore, this study employed a cross-sectional descriptive model, which means that caution should be taken when extrapolating the results to other environments with diverse demographics and clinical management approaches. Nonetheless, it is essential that we conducted further comprehensive investigations to validate our results and to thoroughly evaluate the significance of RV-FWLS in the early detection of cardiac injury among patients affected by COVID-19.

CONCLUSION

Despite the passing of the acute stage of the disease, individuals who have recovered from COVID-19 still exhibit subclinical Right ventricular dysfunction. This was clearly demonstrated by the significant reduction observed in the measured values of RV global longitudinal strain and RV free wall longitudinal strain. Consequently, evaluating RV longitudinal strain provided a precise and reliable assessment of the long-term effects that COVID-19 has on the performance and function of the heart muscle. This assessment can specifically reveal the deterioration of RV GLS and RVFWLS even before the typical 2D echocardiography measurements show any changes. This discovery has substantial ramifications for forecasting the likely outcome or course of a disease or condition.

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