The Egyptian Journal of Hospital Medicine (January 2022) Vol. 86, Page 318-323

Cardiovascular Manifestations in Echocardiography in Patients Recently Recovered From COVID-19 Infection

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ABSTRACT
Background: As a major source of morbidity and mortality, COVID-19 (coronavirus disease 2019) has developed. In both COVID-19 and other pneumonias, high T/I troponin levels may indicate damage to the heart. **Objective**: ln order to expand our understanding of COVID-19 cardiology effects, as well as provide insights into the features of people who are more prone to cardiovascular diseases. **Methods:** At isolation hospital in Zagazig, and the isolation hospital in Tripoli, Libya, 42 COVID-19 positive subjects were studied for their echocardiographic parameters, the study was carried out from March 5th, 2021, to September 4th 2021. **Results:** Arrhythmias, myocardial infarctions, valvular dysfunction, pulmonary hypertension, and right ventricular dysfunction (RVD) were found to have no statistically significant association to the severity of COVID-19. Mean of left ventricular ejection fraction (LVEF) was statistically lower among severe COVID-19 patients than moderate and mild cases but means of RV diameter (mm) was statistically higher among severe COVID-19 patients than moderate and mild cases, mean of fractional area change (FAC) was statistically lower in severe COVID-19 patients. Pulmonary hypertension was the second most common echocardiographic finding (38% of patients). There was no statistically significant difference in pulmonary hypertension across COVID-19 patients in relation to the severity (P=0.211).
Conclusion: Echocardiography can provide us with important information which can help in managing of patients with COVID-19 while we must consider contamination risks as well as transmission of diseases.
Keywords: Coronavirus Disease, Echocardiography.

INTRODUCTION
As a major source of morbidity and mortality, COVID-19 (coronavirus disease 2019) has emerged as a substantial burden on healthcare systems around the world [(1)]. After infecting a person's respiratory system, COVID-19 can progress to cause systemic illness. The virus causes multi-organ dysfunction and failure, with the lungs being the most afflicted and the cardiovascular system following it closely [(2)]. SARS-CoV-2, the virus that causes COVID-19, mostly affects the respiratory system, however people who have a history of cardiovascular illness or have high cardiac biomarkers are more vulnerable and have a worse prognosis [(3)].

For now, we don't know what's going on behind these findings. Acute myocardial infarction has been reported as a possible side effect of COVID-19, according to preliminary case reports [(4)], myocarditis, [(5)] as well as takotsubo cardiomyopathy. Cardiac pathology can cause both acute left and right ventricular failure, with the latter also occurring as the result of an increase in the right ventricular afterload due to pneumonia or pulmonary embolism [(6)].

Chen *et al.* [(7)] and **Varga *et al.*** [(8)] Angiotensin-converting enzyme 2 receptor-mediated systemic endotheliitis has been hypothesized as a pathophysiological mechanism of heart injury, according to a study in the Journal of the American College of Cardiology. T/I troponins and natriuretic peptides may be high in both COVID-19 and other pneumonias, indicating damaged myocardium or increased hemodynamic overload [(9)]. One or two postmortem cases showed the presence of interstitial mononuclear inflammatory cells; this suggests the underlying cause of cardiac inflammation [(10)]. In individuals with cardiogenic shock and COVID-19, virus particles have been found in the heart and vascular endothelium. There is, however, no data on how common these cardiac issues are or how best to treat them or allocate resources in the event that they occur. Because of this, it is imperative that we better understand how COVID-19 and the heart interact [(11)]. As a result of the pandemic, non-invasive diagnostic cardiology services have been restructured to emphasize bedside transthoracic echocardiography (TTE) [(12)].

This study aimed to increase our knowledge of the cardiac manifestations of COVID-19 in people who do not have a history of cardiovascular disease and offer information on the features of persons who are more likely to develop cardiovascular disease.

PATIENTS AND METHODS
At isolation hospital in Zagazig, and the isolation hospital in Tripoli, Libya, 42 COVID-19 positive subjects were studied for their echocardiographic parameters. The study was carried out from March 5th 2021 to September 4th 2021.

Ethical considerations:

As long as all participants signed informed consent forms and submitted them to Zagazig and Tripoli

Received: 27/8/2021
Accepted: 13/10/2021

University's Research Ethics Committee, the study was allowed (ZU-IRB#6693). We followed the World Medical Association's ethical code for human experimentation, the Helsinki Declaration.

Inclusion criteria: Non-cardiac patients. Having suffered COVID-19 illness confirmed by RT-PCR on nasopharyngeal swab or imaging findings (Chest CT scan). Men or women. Age from18 years to 65 years. No history of lung disease. No ongoing or previous cardio or vasoactive treatment. Able to give informed consent, and DM (new diagnosed without treatment).

Exclusion criteria: Patients with recent non COVID - 19 infection. Patient in atrial fibrillation or known coronary artery disease. Pregnancy. Patients with malignancies or inflammatory diseases. Inability to provide consent. Chronic hepatic or renal disease. Diabetes mellitus, and dyslipidemia.

Echocardiograms were performed on 42 patients who were tested positive for COVID-19. Swabs from the nasopharynx were tested for the presence of COVID-19 using real-time reverse transcription polymerase chain reaction (rRT-PCR), patient with CO-RAD scoring equal or more than 4 were included in the study. CO-RAD 1 (no suspicious of COVID-19), CORAD 2 (low suspicious of COVID-19), CO-RAD 3 (intermediate suspicious of COVID-19), CO-RAD 4 (highly suspicious COVID-19), CO-RAD 5 (very highly suspicious of COVID-19).

All patients were submitted to full history taking, clinical examination:

In general, the prevalence of the range of illness severity according to WHO as follows: (1) Respiratory symptoms without signs of pneumonia or hypoxia constitute mild COVID-19. (2) Moderate COVID-19: the presence of clinical and radiographic signs of pneumonia, as well as a room air oxygen saturation (SpO_2) of at least 90%. (3) Severe COVID-19: presence of clinical and radiological evidence of pneumonia, reduced oxygen saturation on room air at sea level, respiratory rate exceeding 30 breaths per minute (bph), or lung infiltration greater than 50% [13].

Echocardiography:

All patients had an echocardiogram. Apical and long-and-short-axis views of the parasternum were the most commonly employed imaging windows. As measured by a parasternal long axis, the left ventricular dimensions. End-diastole and end-systole views of the apical four-chamber and two-chamber views were utilised to trace the endocardial border and calculate LV volumes (EDV and ESV) and EF using the modified Simpson's biplane approach [14]. Diastolic function was assessed through using pulsed-wave (PW) Doppler technique interrogating mitral inflow. Measurement of peak early diastolic velocity (E), peak late diastolic velocity (A), E/A ratio from the transmitral flow signal

*Grade 1 DD A modest diastolic dysfunction or an inability to relax properly may be present): E/A ratio < 0.8, DT > 200 milliseconds, E/e’ equal or less than 8.

*Grade 2 DD (pseudonormal phase or mild diastolic dysfunction): E/A 0.8-1.5, DT 160-200 milliseconds, E/e’ 9-12.

*Grade 3 DD (filling phase restriction or diastolic dysfunction): E/A ratio equal or more than 2, DT less than 160 milliseconds, E/e’ equal or more than a 13.

LVEF was normal in the males and females, ranging from 52 to 72 percent for men and 54 to 74 percent for women, and any evidence of myocardial infarction or the takotsubo cardiomyopathy, a temporary and reversible systolic abnormality of the left ventricle's apical area characterized by an apical ballooning appearance, was recorded on the echocardiogram [15]. Insufficiencies of the right ventricle (defined as a fractional area change less than 35 percent or a TAPSE less than 17 millimeters), TAPSE is an acronym for tricuspid annulus systolic displacement evaluation in M-mode, RV-FAC was computed by tracing the endocardial borders of the RV in diastole and systole in the four-chamber view and recording areas in each cardiac phase, and the difference between the two was expressed as a percentage of end-diastolic RV area, RV dilatation, and D-shaped left ventricle: VTI is a measure of RVOT VTI, which was taken through a parasternal short axis view, PW Doppler sample volume put in the proximal RVOT immediately below the pulmonary valve. This correlates with substantial RV overload, elevated pulmonary artery pressure, SPAP: the tricuspid regurgitation (TR) trace was used to quantify the differential in pressures of the right ventricle and right atrium by utilising the simplified Bernoulli equation p = 4[TRmax]2 to calculate this pressure difference. A pulse wave signal of pulmonic forward flow was used to calculate the mean pap in a parasternal short axis view, just proximal to the pulmonary valve, from the start to the peak flow velocity, the RVOT acceleration time was determined, and a value of less than 100 ms was strongly indicative of pulmonary hypertension.

Statistical analysis

In order to analyze the data acquired, it was loaded into a computer and run via the Statistical Package for the Social Sciences, version 20. (SPSS). The Shapiro–Wilk test was used to examine the distribution properties of variables as well as the homogeneity of variance. The quantitative data were reported in the form of the mean, and standard deviation (SD). The frequency and proportions of qualitative data were used to present the information. For quantitative independent one-way ANOVA was employed to examine the data as needed. To examine qualitatively independent data, researchers employed the Pearson Chi-Square Test. P value equal to or less than 0.05 was regarded as statistically relevant.

RESULTS

Demographic and clinical data are shown in table 1.

Table (1): The study group's demographic characteristics and clinical data

Item		Studied group N= 42	
Age (years)	Mean ± SD	54.98 ± 8.53	
	(Range)	27-65	
Systolic BP (mm Hg)	Mean ± SD	119.24 ± 17.38	
Diastolic BP (mm Hg)	Mean ± SD	70.12 ± 9.39	
Heart rate (beat/min)	Mean ± SD	95.21 ± 18.4	
		No	%
Sex	Female	16	38.1 %
	Male	26	61.9 %

Table (2) shows that about 2/3 of the studied patients had severe COVID-19 disease.

Table (2): Severity of COVID-19 among the studied patients

Item		Studied group N=42	
		no	**%**
Severity of disease	**Mild**	5	11.9
	Moderate	10	23.8
	Severe	27	64.3

38% of studied patients had pulmonary hypertension (Table 3).

Table (3): Pulmonary hypertension among the studied patients

Item		Studied group N=42	
		no	**%**
Pulmonary hypertension	**No**	26	62.0
	Yes	16	38.0

Less than half of the studied patients had no valvular affection (Table 4).

Table (4): Valvular affection among the studied patients

Item		Studied group N=42	
		no	**%**
MR	Negative	34	81.0
	Mild	7	16.7
	moderate	1	2.4
AR	Negative	39	92.9
	Mild	3	7.1
TR	Negative	25	59.5
	mild	8	19.0
	moderate	9	21.4
None	No valvular lesion	20	47.6

Arrhythmias, myocardial infarctions, valvular dysfunction, pulmonary hypertension, and RV dysfunction (RVD) were found to have no statistically significant association to the severity of COVID-19. Mean of LVEF was statistically lower among severe COVID-19 patients than moderate and mild cases. But means of RV diameter (mm) was statistically higher among severe COVID-19 patients than moderate and mild cases, mean of FAC was statistically lower in severe COVID-19 patients. There was not statistically difference regarding other echocardiographic data **(Table 5).**

Table (5): Relation between (ECG findings and echocardiographic data) and COVID-19 severity among the studied patients

Variable		COVID-19 severity						P	Post Hoc
		Mild (N=5)		Moderate (N=10)		Severe (N=27)			
		No	%	No	%	No	%		
Arrhythmias									
▪ APCs		1	20.0	1	10.0	2	7.4	0.677	-
▪ VPCS		0	0.0	2	20.0	2	7.4	0.379	-
▪ S.TACY		4	80.0	4	40.0	15	55.6	0.338	-
▪ LBBB		0	0.0	0	0.0	2	7.4	0.650	-
▪ RBBB		0	0.0	0	0.0	2	7.4	0.650	-
Myocardial infarction									
▪ NSEMI		0	0.0	0	0.0	4	14.8	0.421	-
▪ STEMI		0	0.0	0	0.0	2	7.4		
▪ NONE		5	100.0	10	100.0	21	77.8		
Valvular affection									
▪ Positive		1	20.0	3	30.0	16	59.3	0.120	-
▪ Negative		4	80.0	7	70.0	11	40.7		
Pulmonary hypertension									
▪ No		5	100.0	8	80.0	13	48.1	0.211	-
▪ Mild		0	0.0	2	20.0	8	29.6		
▪ Moderate		0	0.0	0	0.0	6	22.2		
RV dysfunction (RVD)									
▪ No (n=27)		4	80.0	6	60.0	17	63.0	0.727	-
▪ Yes (n=15)		1	20.0	4	40.0	10	37.0		
LV EF (%)	Mean ± SD	36.3 ± 6.00		31.9 ± 3.7		27.1± 6.24		0.003 (S)	0.032*
RVOT VTI (cm)	Mean ± SD	19.7 ± 1.47		19.76 ± 1.93		19.37 ± 2.12		0.875 (NS)	------
FAC (%)	Mean ± SD	51.2 ± 2.16		49.4 ± 4.4		44.92 ± 6.12		0.020 (S)	0.034* 0.024*
RVD (mm)	Mean ± SD	28.6 ± 2.3		30.3 ± 3.68		35.56 ± 7.9		0.033 (S)	0.041* 0.040*
TAPSE (mm)	Mean ± SD	19 ± 1.87		19.7 ± 1.82		18.63 ± 1.8		0.291 (NS)	------

DISCUSSION

Even in the absence of any known cardiovascular risk factors, COVID-19 has the potential to cause cardiac problems. Dynamic abnormalities in the electrocardiogram (ECG), such as left and right ventricular dysfunction, ST-segment elevation, and T wave inversions, have been linked to poor prognosis in patients with COVID-19 [16].

Since coronavirus illness 2019 (COVID-19) is associated with cardiovascular problems, two-dimensional echocardiography can serve as an important bedside tool for assessing cardiovascular abnormalities and hemodynamic status in COVID-19 patients [17]. The noninvasive imaging technique of echocardiography is widely employed in the diagnosis of heart disease. The use of echocardiography is restricted by COVID-19, however, due to the risk of exposure to the researchers. Only in cases where findings were predicted to have a therapeutic advantage were echocardiography used in patients with confirmed or suspected COVID-19, as recommended by both European Association of Cardiovascular Imaging (EACVI) as well as American Society of Echocardiography (ASE) [18].

In our study, mean age was 54.98 ± 8.53 with minimum 27 and maximum 65 years old, and according to the statistical analysis, mild disease patients were statistically younger than those with severe disease, age of studied group in mild cases ranged from 27-57 years old, while the age of studied group in moderate cases ranged from 45-65 years old and in severe cases ranged from 34-65 years old. These findings came in agreement with study by **Zhang *et al.*** [19] that enrolled 112 COVID-19 patients and revealed that, the age ranged from 39-67 years old in non-severe cases and ranged from 57-77 in severe cases, and there was statistically significant difference in relation to severity of disease (P<0.01). This could be due to, aging causes numerous biological changes in immune system, which are linked to age related illness and susceptibility to infectious disease

In our study, 2/3 of studied group were males (61.9%), while females were 38.1%. Males and females had no statistically significant differences in illness severity, as 69.2% of male were in severe status vs 56.3% of female in severe status. **Barman *et al.*** [20] enrolled 90 COVID-19 patients, 54% of patients were males and 47% of patients were females and showed that men and women had no statistically significant differences in the severity of symptoms (p=0.524).

Our study, demonstrated that valvular affection was the most common echocardiography finding, which presented in 52% of the studied patients. The severity of COVID-19 was not substantially different between the studied groups. Valvular affection was found in 20% of mild cases, 30% of moderate cases and 59.3% of severe cases. Tricuspid regurgitation was the most common finding followed by mitral and aortic regurgitation. These findings came in agreement with **Khan *et al.*** [21] who showed that the most common abnormality was valve regurgitation, tricuspid regurgitation was the most common observed (56.5%), followed by aortic regurgitation (28.3%) and mitral regurgitation (26.1%). This could be due to direct injury to myocyte, fulminant myocarditis or myocardial infarction resulting in chordae rupture as reported by **Khanduri *et al.*** [22].

Our results revealed that the second most common echocardiography finding was pulmonary hypertension, which represented 38% of patients. In fact, prior research has indicated that the presence of a pH is a risk factor for poor outcomes in ICU treatment. A statistically insignificant difference was found between the two groups in terms of the severity of COVID-19, pH (P= 0.211) and RV dysfunction (P=0.727) [22]. These findings came in different with **Zhang *et al.*** [19] of 112 individuals with COVID-19, 20.9% had severe pulmonary hypertension, while only 2.2% of patients with mild to moderate disease had this complication. This difference was statistically significant from the baseline values of the groups. (P<0.01).

This difference from our result could be due to that we excluded all risk factors and chronic obstructive pulmonary disease (COPD), which can affect our results, while **Zhang *et al.*** [19] didn't exclude it and chronic obstructive pulmonary air way was present in 3.6% of patients, hypertension was present in 32.1% of patients, diabetes mellitus was present in 17% of patients, coronary heart disease was present in 13.4% of patients, atrial fibrillation was present in 3.6% of patients, which may affect the result.

In this study, mean of LVEF was statistically lower among severe patients than moderate and mild cases (P=0.032), mean EF in mild cases ranged from (62-71%), mean EF in moderate cases ranged from (54-74%), mean EF in severe cases ranged from (40-75%). These findings came in agreement **Barman *et al.*** [20] that enrolled 90 patients hospitalized for COVID-19, Patients in the severe group had a lower LVEF than those in the non-severe group, according to the study (LVEF, 61.9% ± 4.8 vs 54.0 ± 9.8% P<0.001).

In our study, there was statistically significant difference in age and there was no statistically significant difference in sex between COVID-19 patients with pulmonary hypertension (PH) and patients with no pulmonary hypertension. These findings came in agreement with **Pagnesi *et al.*** [23], this observational, cross-sectional study enrolled 211 COVID-19 patients, winch revealed that there was statistically significant difference in age (P<0.001) and there was no statistically significant difference in sex (P=0.089) between patients with pulmonary hypertension and patients with no pulmonary hypertension.

CONCLUSION

The echocardiography abnormalities described in our study are varied and there appear to be multiple mechanisms involved. Among patients with abnormal echocardiogram the most frequent abnormality was valvular regurgitation followed by pulmonary hypertension. LV systolic function was normal in most patients, whereas LV diastolic dysfunction was frequently observed. Echocardiography can provide us with important information which can help in managing of patients with COVID-19 while we must consider contamination risks as well as transmission of disease.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.

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