

## Original Research Article

# Transthoracic echocardiographic analysis of moderate to severe COVID-19 patients admitted to ICU at tertiary hospital in India

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## ABSTRACT

**Background:** To describe the transthoracic echocardiographic findings of moderate to severe COVID-19 patients admitted to ICU.

**Methods:** We studied the transthoracic echocardiographic findings performed within 48 hours on admission to ICU of 426 moderate to severe COVID-19 patients from July 2020 to September 2020 during their course of treatment. Echocardiographic study included left ventricular (LV) systolic and diastolic function, left ventricle wall motion abnormalities and right ventricular (RV) assessment.

**Results:** The median age of patients was 58.2 (range 19 to 92 years) and majority of patients were male (71%). Pre-existing comorbidities were reported in 95.5% of patient's, majority being hypertension (42.7%) and diabetes mellitus (39.2%). Abnormal echo findings were noted in 40.8% (n=174) with majority of abnormal findings noted in age group of 60-69 (n=54), men (n=114) and in patients with pre-existing coronary artery disease (CAD) (n=28). The common pattern of cardiac abnormalities was LV systolic dysfunction (n=73, 17.1%), RV dysfunction (n=30, 7%) and abnormal PA pressures (n=144, 85.2%). Abnormal echo findings were noted in 46% of patients who died and 33.9% of patients who required hospital stay of more than 10 days.

**Conclusions:** Forty percent of admitted patients to ICU had abnormal echocardiography findings with around eighty five percent of them having raised pulmonary artery pressures. Trans-thoracic echocardiography could be used as a prognostication tool of patients admitted to COVID ICU.

**Keywords:** COVID-19, Trans-thoracic echo, LV dysfunction, RV dysfunction

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by single strand enveloped virus coronavirus 2 (SARS-CoV-2) has severely impacted healthcare systems all over the world. Apart from involvement of lungs, myocardial damage leading to significant cardiac and endothelial dysfunction both in patients with pre-existing cardiac ailments and new onset cardiac dysfunction in patients infected with COVID 19 has been documented.<sup>1-5</sup> The pattern of cardiac involvement maybe either due to direct insult to the myocardium causing viral myocarditis, acute

coronary syndrome (ACS) either due to plaque rupture or coronary thrombosis or as a sequelae to various medications used during the treatment for virus like hydroxychloroquine etc.<sup>6-15</sup> The first COVID positive patient was admitted at our hospital on 22 March 2020 and since then, many moderate to severe hypoxic COVID patients have been managed at our intensive care unit (ICU). Trans-thoracic echocardiography is an inexpensive, non-invasive, bedside portable tool which can be used to identify and quantify various cardiac abnormalities. Over the last few months numerous studies have been published describing the echocardiographic

findings among patients infected with COVID-19.<sup>16-20</sup> In our study, we presented the transthoracic echocardiographic analysis of 426 moderate to severe COVID-19 patients admitted at our ICU from July 2020 to September 2020 during their course of treatment.

## METHODS

### Study overview

The study was conducted by the department of cardiology and critical care medicine in a tertiary care hospital located in Pune, India. The study was approved by the Institutional Ethics Committee and owing to the retrospective observational nature of the study, waiver of informed consent was obtained vide DMHRC code IHR\_2020\_Jul\_PM\_374.

### Procedure

All the COVID positive patients admitted to our ICU at Deenanath Mangeshkar Hospital and Research Centre, Pune, India had undergone echocardiographic screening within 48 hours of their admission. Four hundred twenty six moderate to severe COVID-19 who met the inclusion criteria and underwent bedside echocardiographic evaluation were included in our study. Echocardiographic study included left ventricular (LV) systolic and diastolic function, left ventricle wall motion abnormalities and right ventricular (RV) assessment

### Inclusion criteria

COVID-19 positive patients either by RT-PCR or rapid antigen, Moderate to severe hypoxia  $\text{PaO}_2/\text{FiO}_2 < 200$  or  $\text{SpO}_2/\text{FiO}_2 < 200$  and patients requiring any form of oxygen support and admission to intensive care unit.

### Exclusion criteria

Patients less than 18 years of age and patients admitted with advance directives for palliative care.

Standard of care, such as antivirals, steroids, and anticoagulants, were administered apart from oxygen supplementation by nasal cannula, nonrebreather mask (NRBM), high flow nasal cannula (HFNC), non-invasive ventilation (NIV) or invasive mechanical ventilation as per the hospital protocol. Bedside trans-thoracic echocardiography was performed within 48hrs of admission of patients to ICU as per the discretion of treating physician and clinical indication including haemodynamic deterioration, elevation in cardiac biomarker levels or in patients with pre-existing cardiac comorbidities.

The sonographers performed the bedside scans overcoming many odds including risk of infection to self and restricted mobility after donning PPE, poor echo windows due to limited manoeuvring and poor

cooperation from anxious and severely hypoxic patients, many of them requiring Non-Invasive ventilation and invasive ventilation on COVID awake repositioning protocol (CARP) and prone ventilation.

### Data source

Demographic, clinical, laboratory and echocardiographic data of 426 patients who met the inclusion criteria admitted between July 2020 to September 2020 was collected. The collected data were analysed and interpreted by two independent intensivists and cardiologist. Echocardiography- dedicated equipment Philips CX 50 with a S5-1 (1-5MHz) cardiac probe allowing M-mode and two-dimensional measurements was earmarked for all patients admitted to ICU. Bedside transthoracic echocardiography was performed by echo technicians with expertise in echocardiographic recording using standard PPE and laid down infection control practices of the hospital. The echo recordings were interpreted by cardiologists.

The equipment was thoroughly disinfected after scanning of each patient. Parasternal Long axis, parasternal short axis and apical 4 chamber views were used and the following data was obtained (Figure 2-4). Since no standard guidelines or definitive echocardiography data exists on patients pertaining to COVID-19 patient's standard reference values of patients published prior to COVID pandemic was taken for comparison.<sup>21-23</sup> Left ventricular dysfunction was defined as a left ventricular ejection fraction (LVEF)  $< 50\%$ , whereas right ventricular dysfunction was defined with a TAPSE measurement  $\leq 16$  mm and ESPAP  $> 36$  mmHg was defined as pulmonary hypertension. Abnormal echo findings and cardiac dysfunction was considered to be present in case of left or/and right ventricular dysfunction and presence of pulmonary hypertension.

### Left ventricle (LV)

LV diameters, volumes, ejection fraction (LVEF). Measurements of mitral inflow; Peak early filling (E wave), late diastolic filling (A wave) velocities, E/A ratio, deceleration time of early filling velocity. Early diastolic mitral septal and lateral annular velocities ( $e'$ ) were measured in the apical 4-chamber view. Left atrial volume was calculated with the biplane area-length method at end systole. Forward stroke volume was calculated from the LV outflow tract with subsequent calculation of cardiac output and index

### Right ventricular (RV)

Right ventricle (RV), end-systolic and end-diastolic RV areas and tricuspid annulus were measured. (4 chamber view). RV function was evaluated by tricuspid annular plane systolic excursion, systolic tricuspid lateral annular velocity (RVS) measured in the apical 4-chamber view.

### Statistical data analysis

The data on categorical variables is shown as n (% of cases) and the data on continuous variables is presented as median and IQR (Inter quartile range). The inter-group statistical comparison of distribution of categorical variables is tested using Chi-Square test or Fisher's exact probability test if more than 20% cells have expected frequency less than 5. The inter-group statistical comparison of medians of continuous variables is done using Mann-Whitney U test. All results are shown in tabular as well as graphical format to visualize the statistically significant difference more clearly. In the entire study, the p values less than 0.05 are considered to be statistically significant. The entire data is statistically analysed using statistical package for social sciences (SPSS ver 22.0, IBM Corporation, USA) for MS Windows.

### RESULTS

A total of 426 patients met the inclusion criteria during the study period. The age of patients ranged from 19 to 92 years (mean 58.2±13.7) and majority of patients were male (71%). Pre-existing comorbidities were reported in 95.5 % of patient's, majority being hypertension (42.7%)

and diabetes mellitus (39.2%) (Table 1). Abnormal echo findings were noted in 40.8% (n=174) with majority of abnormal findings noted in age group of 60-69 (n=54), men (n=114) and in patients with pre-existing CAD (n=28) (Table 2).

### Pattern of cardiac disease on trans-thoracic echo

The common pattern of cardiac abnormalities noted in patients with COVID 19 on trans-thoracic echocardiography were LV systolic dysfunction (n=73, 17.1%), RV dysfunction (n=30, 7%) and abnormal PA pressures (n=144, 85.2%) (Table 2, Figure 1).

### Biomarkers vs. echocardiography findings

Levels of biomarkers were analysed among patients with abnormal Echo findings. Troponin T levels were elevated above 99 percentile in 27.8% of patients (23 out of 68 patients) in patients with abnormal echo findings vs 19.1% (9 out of 47 patients) in patients with normal echo in whom the test was done. Hs CRP levels were raised in 93.3% (153 out of 164 patients) and D-Dimer was raised in 89.9% (133 out of 148 patients) in patients with abnormal echo findings which is statistically significant (p<0.05) (Table 3 and 4).

**Table 1: Demographic data of hospitalized patients with coronavirus disease.**

Parameters	Normal echo (n=252)		Abnormal echo (n=174)		Total (n=426)		P value	
	Frequency	%	Frequency	%	Frequency	%		
Age group (years)	<30	10	4.0	0	0.0	10	2.3	0.073
	30-39	22	8.7	16	9.2	38	8.9	
	40-49	34	13.5	26	14.9	60	14.1	
	50-59	71	28.2	38	21.8	109	25.6	
	60-69	62	24.6	54	31.0	116	27.2	
	70-79	42	16.7	35	20.1	77	18.1	
	≥80	11	4.4	5	2.9	16	3.8	
Sex	Male	192	76.2	114	65.5	306	71.8	0.016*
	Female	60	23.8	60	34.5	120	28.2	
Co-morbidity	Hypertension	106	42.1	76	43.7	182	42.7	0.741
	Diabetes mellitus	95	37.7	72	41.4	167	39.2	0.444
	CAD	10	4.0	28	16.1	38	8.9	0.001***
	CKD	9	3.6	9	5.2	18	4.2	0.419
	Other	1	0.4	1	0.6	2	0.5	0.999

Note: P value by Chi-square test. P value<0.05 is considered to be statistically significant. \*P value<0.05, \*\*\*P value<0.001.

**Table 2: Pattern of cardiac disease in hospitalized patients with coronavirus disease.**

Parameters	N	%	
LV systolic function	Normal	353	82.9
	Abnormal	73	17.1
RV function	Normal	396	93.0
	Abnormal	30	7.0
PA pressures	Normal (absent)	25	14.8
	Abnormal (present)	144	85.2
Overall (echo)	Normal	252	59.2
	Abnormal	174	40.8

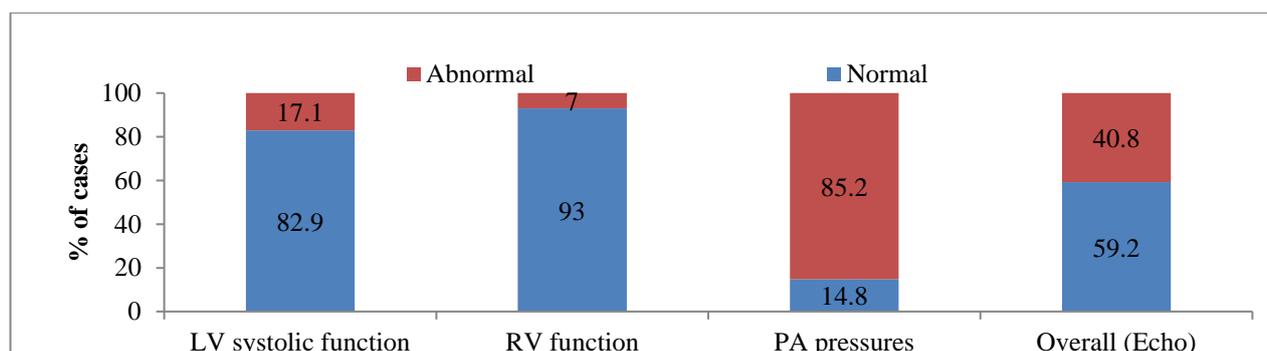


Figure 1: Pattern of cardiac disease in hospitalized patients with coronavirus disease.

Table 3: Distribution of average levels of biomarkers according to echocardiographic status among the hospitalized patients with coronavirus disease.

Biomarkers	Normal echo		Abnormal echo		Total		P value
	Median	IQR	Median	IQR	Median	IQR	
Trop-T (n=47/n=68)	0.030	0.00	0.030	0.058	0.030	0.019	0.059
Sr Ferritin (n=153/n=123)	420.00	560.82	583.38	797.27	472.80	726.80	0.022*
Hs-CRP (n=217/n=164)	75.67	125.30	123.32	138.47	90.46	142.89	0.001***
IL6 (n=77/n=52)	36.60	124.35	66.95	151.02	49.10	123.60	0.128
D-Dimer (n=188/n=148)	895.82	1055.46	1237.20	1677.12	999.95	1317.51	0.001***

Note: IQR-Inter quartile range. P value by Mann-Whitney U test. P value<0.05 is considered to be statistically significant. \*P value<0.05, \*\*\*P value<0.001.

Table 4: Distribution of abnormal levels of biomarkers according to echocardiographic status among the hospitalized patients with coronavirus disease.

Biomarkers		Normal echo		Abnormal echo		Total		P value
		N	%	N	%	N	%	
Trop-T	Normal	38	80.9	45	66.2	83	72.2	0.084
	Abnormal	9	19.1	23	33.8	32	27.8	
Sr. Ferritin	Normal	74	48.4	49	39.8	123	44.6	0.157
	Abnormal	79	51.6	74	60.2	153	55.4	
Hs-CRP	Normal	28	12.9	11	6.7	39	10.2	0.048*
	Abnormal	189	87.1	153	93.3	342	89.8	
IL6	Normal	6	7.8	2	3.8	8	6.2	0.473
	Abnormal	71	92.2	50	96.2	121	93.8	
D-Dimer	Normal	38	20.2	15	10.1	53	15.8	0.012*
	Abnormal	150	79.8	133	89.9	283	84.2	

Note: P value by Chi-square test (Fisher's exact probability test). P value<0.05 is considered to be statistically significant. \*P value<0.05.

Table 5: Distribution of outcome according to echocardiographic status among the hospitalized patients with coronavirus disease.

Outcome	Normal echo (n=252)		Abnormal echo (n=176)		Total (n=428)		P value
	N	%	N	%	N	%	
Discharge <10 days	96	38.1	35	20.1	131	30.8	0.001***
Discharge >10 days	91	36.1	59	33.9	150	35.2	
Death	65	25.8	80	46.0	145	34.0	
Total	252	100.0	174	100.0	426	100.0	

Note: P value by Chi-Square test. P value<0.05 is considered to be statistically significant.

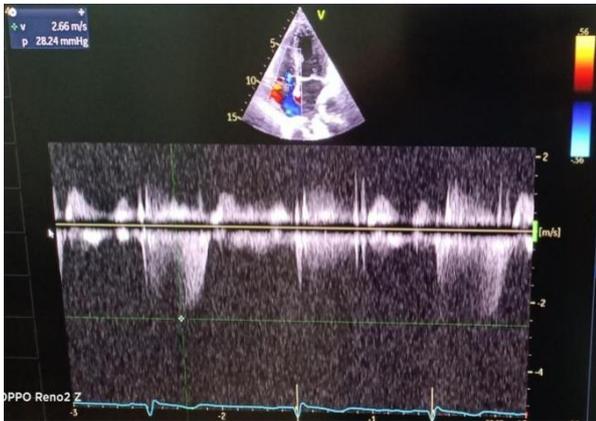
**Outcome of treatment vs. echocardiographic findings**

Abnormal echo findings were noted in 46% of patients who died and 33.9% of patients who required hospital stay of more than 10 days. 38.1% (96 out of 131 patients) who were discharged within 10 days had normal echo findings which is statistically significant (Table 5).

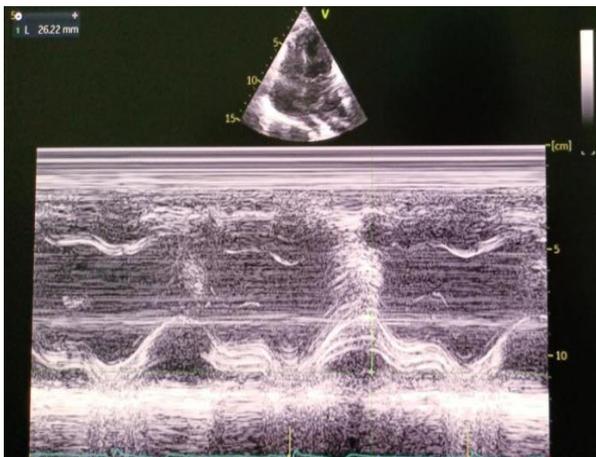
**DISCUSSION**

Over the last few months numerous observational studies, case series and case reports from all over the globe have described and quantified the cardiovascular manifestations in patients infected with COVID-19 both in patients with and without pre-existing cardiovascular diseases.<sup>1-15</sup> Multitude of cardiovascular manifestations have been described on transthoracic echocardiography performed electively on all patients or on those with clinical indications with varied frequency of involvement of left ventricle, right ventricle and pulmonary artery pressures.

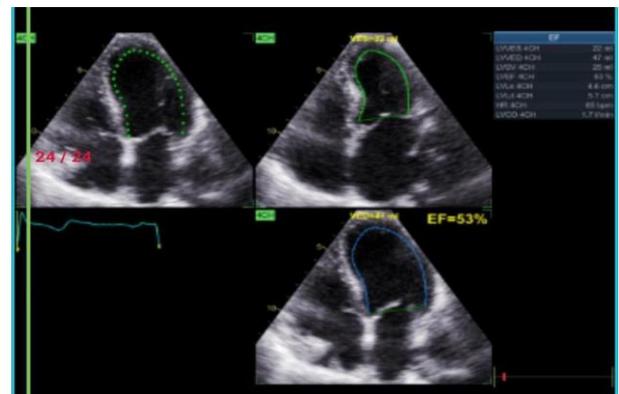
This retrospective study would be to our knowledge one of the largest studies from India which describes the trans-thoracic echocardiographic findings of moderate to severe hypoxic COVID-19 patients requiring any form of oxygen support admitted to ICU. Being a resource limited setting with huge deluge of patients many investigations including biochemical parameters and cardiac biomarkers could not be done in all the patients. During our study, we noticed that around forty percent of admitted patients had abnormal echo findings with around eighty-five percent of them having raised pulmonary artery pressures. Majority of abnormal findings were noted in age group of 60-69 (n=54), men (n=114) and in patients with pre-existing CAD (n=28). Around half of the patients who succumbed to the illness had an abnormal echo finding.



**Figure 2: Measurement of tricuspid valve regurgitation jet gradient for assessment of pulmonary artery systolic pressure.**



**Figure 3: Measurement of tricuspid annular peak systolic excursion (TAPSE) for assessment of right ventricular systolic function.**



**Figure 4: Semi-automated measurement of LV ejection fraction (LVEF).**

In current study cohort more than 85% of patients had elevated Pulmonary artery pressures much higher than those noted in other studies while RV dysfunction was noticed in 7%, much less than 33% reported by Dwerck et al 40.3% by Jain et al and 27% by Elsayed et al.<sup>16-20</sup> Similarly, 17% of patients in our cohort had LV systolic dysfunction (LVEF <50%) the numbers of which are much less than 37% reported by Dwerck et al and 34.7% by Jain et al and around 10% by Szekely et al.<sup>18</sup> The significant variation in Echo findings including elevated numbers in pulmonary artery pressures compared with other studies could be explained by the fact that all the patients in our cohort were confirmed COVID-19 moderate to severely hypoxic patients admitted to ICU, requiring some form of oxygen therapy though the exact mode of oxygen support (Face mask, NIV or IMV) and the day of illness has not been documented. Also, similar to study by Szekely et al all our patients underwent bedside echocardiography screening within 48 hrs of their admission to ICU irrespective of any clinical indication, vis a vis the patients in studies by Dwerck et al and Jain et al underwent screening only on definitive clinical indication.<sup>17-19</sup>

Also, median values of biomarkers Hs-CRP (123 mg/l) and D-Dimer (1237 ng/ml) were raised in patients with

abnormal echo. No individual correlation of the same was done with either LV or RV dysfunction by us, unlike Jain et al who noticed a weak inverse relationship between Hs-cTnT and LVEF and Dwerck et al reported that patients with biomarker elevation (69%) were more likely to have an abnormal echocardiogram. No relation between Troponin or BNP elevation and RV abnormalities was noted while troponin elevation predicted LV abnormalities on echocardiogram. In our study abnormal echo findings were recorded in 46% of patients who died and 33.9% of patients who required hospital stay of more than 10 days. This would indicate that an overwhelming number (almost 4 in 5) of patients with moderate to severe COVID-19 and abnormal echocardiography findings had a subsequent adverse outcome or required prolonged hospital care. This is crucial information in the context of the overwhelming burden of the COVID pandemic in resource constrained settings. Echocardiography being a common non-invasive investigation tool available in most ICU's, we suggest that Trans-thoracic echocardiography could be used a prognostication tool for mortality in patients admitted to COVID ICU.

### Limitations

Limitations of current study were first, this was a retrospective observational study carried out in a single centre with all its inherited biases. Secondly, high heterogeneity in the study group due to non-uniformity in the selection of the study subjects due to participant's inclusion criteria as well as by the study design, limited investigations conducted due to huge deluge of patients and also cost constrains making the data redundant for comparative analysis. Third, though the pre-existing comorbidities were documented and comparison with prior available echocardiographic findings in the hospital database was made during patient care, the same has not been documented in our study. Fourthly, repeat scans conducted on individual patients with worsening clinical condition to study the progress of clinical deterioration were not included in the study.

### CONCLUSION

Affliction of cardiovascular system has been reported in a significant number of patients with COVID-19. In our study cohort consisting of all patients admitted to ICU with moderate to severe hypoxia around forty percent of admitted patients had abnormal echo findings with around eighty five percent of them having raised pulmonary artery pressures. The number of patients with abnormal biomarker levels and raised median values of biomarkers was more in people with abnormal echo compared to those with normal. Trans-thoracic echocardiography could be used a prognostication tool of patients admitted to COVID ICU.

### Recommendations

Serial echocardiographic studies looking at time course for the development of these cardiac abnormalities and correlation with biomarkers would be worthwhile. Advanced measurements of the Right and left ventricle particularly strain pattern and 3D images correlating with disease severity. Future studies, involving multiple centres, larger sample sizes, and international collaboration, are needed to determine the true prognostic value of echocardiographic parameters in patients with COVID-19 infection and allow for further refinement of stratification by determinants such as age, sex and ethnicity.

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