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A REVIEW OF RIGHT VENTRICULAR ECHOCARDIOGRAPHIC PARAMETERS IN COVID-19 PATIENTS AND RELATION WITH DISEASE OUTCOMES

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Abstract:

Introduction: *Coronavirus Disease 2019 (COVID-19) primarily manifests with respiratory symptoms. However, it leads to increased mortality due to multi-organ involvement, among which the cardiovascular system is of paramount importance in determining the mortality and morbidity of COVID-19 patients. Echocardiography plays a crucial role in assessing cardiac function in COVID-19 patients. Our objective is to discuss the echocardiographic findings related to the right ventricle and their significance in the clinical outcomes of COVID-19 patients.*

Methodology: *We conducted a systematic search in PubMed, Scopus, and Google Scholar databases. A total of 8 studies were selected for review. We included original studies published between 2020 and 2022. Only studies involving hospitalized COVID-19 patients were considered.*

Results: *We identified 9 studies related to the echocardiographic evaluation of cardiac manifestations. Right ventricular alterations were examined in these studies, and the findings were categorized under the headings of anatomical and functional parameters of the right ventricle. The studies reported increased mortality in association with abnormal TAPSE and sPAP. RV-FAC was associated with increased admissions to the ICU. Among the anatomical parameters of the right ventricle, an increase in RVD was linked to increased mortality.*

Conclusion: *This review suggests that identifying echocardiographic parameters related to COVID-19 is crucial. Alterations in the functional parameters of echocardiography have greater prognostic value than anatomical parameters. Targeting such parameters will help avoid unnecessary investigations.*

Key Words: Covid-19, cardiac dysfunction, corona, Echocardiography, Right ventricle

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INTRODUCTION:

In December 2019, an outbreak began, later named the Coronavirus pandemic or COVID-19 pandemic. The disease primarily affects the respiratory system, with symptoms ranging from mild flu-like illness to severe pneumonia, often accompanied by acute respiratory distress syndrome (ARDS), respiratory failure (RF), and multi-organ involvement [1]. Increasing evidence suggests that the heart is a crucial target in this disease [2]. The respiratory and cardiovascular systems are considered the most critical factors in predicting morbidity and mortality in COVID-19 [3]. COVID-19 appears to impact the cardiovascular system in various ways, with heart failure, arrhythmias, and myocardial infarctions increasingly reported in COVID-19 patients [4]. The frequency of cardiac injury is estimated at 20% to 30% in coronavirus patients and serves as a significant indicator of poor prognosis [1]. The role of echocardiography is vital in the initial evaluation of heart function in COVID-19 patients. Many studies have investigated cardiac issues in COVID-19 patients using echocardiography, both in acutely ill cases and in examining long-term complications. Echocardiography is an easily accessible and cost-effective method for evaluating severely ill patients, providing valuable information about the structure and function of the heart (5). Due to the contagious nature of COVID-19 and the risk of equipment contamination and staff exposure, top echocardiographic societies suggest using echocardiograms only when the information obtained can be expected to provide a therapeutic advantage. They also recommend using smaller, easier-to-disinfect portable devices and conducting focused assessments rather than full echocardiograms [6, 7]. In COVID-19 patients, hypoxia leads to alveolar damage and an increase in pulmonary vascular resistance, causing elevated right ventricular (RV) afterload. Right ventricular abnormalities are part of a cascade of events that ultimately worsen acute respiratory distress syndrome (ARDS) in these patients [8]. Timely detection of these cardiac changes is possible with echocardiography if we identify echo parameters strongly associated with disease outcomes and focus our investigations on the most beneficial parameters, thereby avoiding unnecessary exposure of staff and equipment to COVID-19 patients.

In this review, we will discuss different echocardiographic parameters used to evaluate the right side of the heart and study their association with disease outcomes in COVID-19 patients.

METHODOLOGY:

We conducted a comprehensive systematic search using the search engines PubMed, Scopus, and Google Scholar. Initially, a total of 25 studies were identified. Only original research studies involving COVID-19 patients were included in our analysis. Articles containing data from outpatient departments were excluded from the study. Additionally, studies exclusively focused on left ventricular findings in echocardiography were excluded from the review. Ultimately, we selected 9 studies for the review.

Anatomical Echocardiographic parameters of right side of heart:

Several echocardiographic parameters are employed for the anatomical assessment of the right ventricle (RV). These include linear dimensions of the RV, RV wall thickness, and RV area. Regarding linear dimensions, measurements are taken at both the basal and mid-cavity levels. RV dilatation is defined as an RV diameter greater than 41mm at the basal level and more than 35mm at the mid-level, as observed in an RV-focused view [9]. Another parameter used to assess RV dilatation is the ratio of RV end-diastolic area to left ventricular (LV) end-diastolic area, which should be greater than 0.6. Although this parameter primarily reflects RV systolic function [10], in this study, we will discuss it within the category of anatomical parameters of the RV since it is used to indicate RV dilatation, an anatomical abnormality.

Right Ventricular Diameter (RVD):

Right ventricle diameter (RVD) ≥42mm was observed in 13 patients (14%) out of a total of 90 patients with COVID-19 in a study conducted by Hasan Ali et al. This was a single-centre-based study, and two-dimensional Transthoracic echocardiography (TTE) was used for cardiac evaluation, while the diagnosis of COVID-19 was confirmed by the results of real-time reverse-transcription polymerase chain reaction (RT-PCR) testing [8]. The participants were divided into two groups based on the severity of the illness: the severe group (n=44) and the non-severe group (n=46). The frequency of RV dilatation was higher in the severely ill group (25%) compared to the non-severe group (4%), showing a significant difference (P value=0.007). When disease complications were assessed in the two groups, pericardial effusion was found to be much more frequent in the severely ill group (23%) compared to the non-severe group (0%). However, follow-up data for the patients were not provided in this study [8].

In another retrospective cohort study conducted during March-April 2020, Mahmoud-Elsayed et al. reported RV dilatation in 40.5% of COVID-19 patients (30 out

of 74) with an RV basal diameter >41mm. Most of these patients were admitted with COVID-19 pneumonia and were referred for TTE when they complained of chest pain, an abnormal electrocardiogram (ECG), or arrhythmias. Out of the total 74 patients, 28 patients had died, of which 13 (46.5%) had right ventricular dilatation [11].

Yingxian Liu et al. reported dilated right heart in 53.5% of COVID-19 patients (23/43) with RVD ≥42mm. For cardiac evaluation of these patients, two-dimensional echocardiography was used. These patients were COVID-19 positive and diagnosed with acute respiratory distress syndrome (ARDS). After a mean follow-up period of 33 days, 22 deaths were recorded, and out of the total deaths, 18 (81%) had RV dilatation [12].

In another prospective study, Hemant Chaturd et al. reported a significant increase in RVIDd after a 3-month follow-up period in moderate to severely ill COVID-19 patients compared to the baseline values (38.6 ± 2.1 vs 36.4 ± 2.6). Patients were divided into a mild-COVID-19 group (n=297) and a moderate to severe COVID-19 group (n=335). Mildly ill patients had RVIDd >42 in only 1.3% of cases, while this frequency was found to be 5.1% in the moderate to severe group of COVID-19 patients, reflecting the impact of COVID-19 severity on the dimensions of the right-sided heart [13]."

Right ventricular end-diastolic area/left ventricular end-diastolic area ratio (RVEDA/LVEDA):

Right ventricular dilatation can also be described in terms of the ratio of right ventricular end-diastolic area to left ventricular end-diastolic area (RVEDA/LVEDA). Stephan Huang et al. reported dilated right ventricles based on the RVEDA/LVEDA ratio. Out of a total of 521 patients, 50% (n=262) had an RVEDA/LVEDA ratio greater than 0.6, suggesting right ventricle dilation. Both transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE) were used to examine the patients. Acute cor pulmonale (ACP) was diagnosed when RVEDA/LVEDA was greater than 0.6 and accompanied by evidence of paradoxical septal motion [14].

Saga Jason et al. also evaluated RVEDA/LVEDA in critically ill COVID-19 patients in a retrospective cohort study conducted in Sweden. A total of 74 patients with positive SARS-CoV-2 infection, who underwent echocardiography within the first 72 hours of hospital admission, were included for data collection. RVEDA/LVEDA was found to be within the normal limit in all participants (RVEDA/LVEDA = 0.5). When survival was assessed in these patients, the group with RV dysfunction (n=13) showed a 7.7% ICU mortality rate and a 15.4% mortality rate at a 30-day follow-up. However, no statistical difference was found between the group with RV dysfunction and the normal RV group [15].

In another prospective cross-sectional study conducted in mechanically ventilated patients, Emilio Daniel et al. examined the RVEDA/LVEDA ratio. Participants were diagnosed as COVID-19 positive based on PCR testing and were included in the study if they had undergone mechanical ventilation (MV) within the first 24 hours of admission. An apical 4-chamber view was used to assess RVEDA and LVEDA, with an RVEDA/LVEDA ratio greater than 0.6 indicating a dilated right ventricle. Patients with both right ventricle dilation and paradoxical septum movement were defined as having Acute Cor pulmonale (ACP). Out of a total of 140 patients, the RV was found to be normal in 86 patients with a mean RVEDA/LVEDA ratio of 0.5, while 54 patients were included in the group with RV dilation (RVEDA/LVEDA > 0.6). These patients were further divided into two subgroups: RV dilation only (n=34) and ACP (n=20), with mean RVEDA/LVEDA ratios of 0.7 and 0.9, respectively. The values were consistent with a high mortality rate of 70% (14 out of 20) in ACP patients. However, the mortality rate was 9% (3 out of 34) in patients with "RV dilation only," compared to 27% (23 out of 86) in patients with a normal RV as assessed by the RVEDA/LVEDA ratio. This finding can be attributed to the high prevalence of myocardial infarction, chronic heart failure, COPD or Asthma, and Diabetes Mellitus, and it underscores the potential role of co-existing illnesses in predicting the outcome of COVID-19 patients with cardiac abnormalities [16].

Table#1: Echocardiographic parameters of Right Ventricle showing the anatomical impairments

Anatomical echocardiography parameters of Right ventricle				
	RVD≥42 mm	**Disease Outcome**		
		%Mortality*	**Hospital stays**	**Other Complications**
Hasan Ali et al	14% (13/90)			Pericardial effusion in 23%
Mahmoud-Elsayed et al	40.5% (30/74)	46.5%		
Yingxian Liu et al	53.5% (23/43)	81%		
	RVEDA/LVEDA>0.6			
Emilio Daniel et al	38.5% (54/140)			Pulmonary embolism 63%

RVD= Right Ventricular Dilatation. RVEDA/LVEDA=Right Over left ventricular end diastolic area

*Represents mortality calculated out of total numbers of deaths

Function echocardiographic parameters of Right Ventricle:

Various parameters are employed for the analysis of right ventricular systolic function, with common ones including Tricuspid Annular Plane Systolic Excursion (TAPSE), Right Ventricular Fractional Area Change (RV-FAC), and Right Ventricular Ejection Fraction (RV-EF) [9]. Systolic Pulmonary Arterial Pressure (sPAP) provides details about pulmonary hypertension, which, in turn, is associated with right ventricular functional abnormalities [17].

Tricuspid Annular Plane Systolic Excursion (TAPSE):

Tricuspid Annular Plane Systolic Excursion (TAPSE) is a vital echocardiographic parameter used to assess the functional status of the right ventricle. TAPSE has proven to be a valuable prognostic marker in various cardiac conditions, such as heart failure. It represents the longitudinal shift of the tricuspid ring in the right ventricle, measured using an apical four-chamber image and M-mode ultrasound method, typically scored for accuracy [18]. A TAPSE value below 17mm is typically considered indicative of right ventricular systolic abnormality [9].

Hasan Ali et al. reported TAPSE findings in COVID-19 patients measured using transthoracic two-dimensional (TTE) echocardiography. They recruited a total of 90 patients, dividing them into severe (n=44) and non-severe (n=46) groups based on the severity of COVID-19 symptoms. TAPSE values of 16 mm or less were considered abnormal and suggestive of RV dysfunction. In the non-severe group, 8% of individuals had abnormal TAPSE values compared to 25% in the severe group. However, there was no significant difference in TAPSE values between the two groups. A notable limitation of this study was the absence of a control group for comparison, impacting the significance of the study's results [8].

In another study conducted from January to April 2020, critically ill COVID-19 patients in a newly built Intensive Care Unit (ICU) in Wuhan were evaluated for their cardiac function. Two-dimensional echocardiography with an apical and 4-chambered view was used. A total of 43 patients were enrolled, and after a median follow-up period of 33 days, two groups were compared: survivors (n=21) and non-survivors (n=22). Among the non-survivors, 12 patients had a TAPSE of less than 17mm, with a mean value of 16.3 ± 2.2, compared to a TAPSE value of 21.8 ± 2.9 in survivors. This significant difference in TAPSE values between deceased patients and survivors indicated deteriorated RV systolic function in COVID-19 patients and underscored the reliability of this echocardiographic parameter in assessing cardiac abnormalities [12].

Emilio Daniel et al. reported a normal mean TAPSE value of 21 in the COVID-19 patient group with normal RV (n=86) compared to a mean TAPSE value of 16 in the group of patients with RV dilation + ACP (n=20). There was also a significant difference in TAPSE values between patients with RV dilation only (n=34) and patients with both RV dilation and ACP ($P < 0.05$). The high mortality rate (70%) in ACP patients correlated with the low TAPSE value in these patients. However, the low mortality rate (9%) in RV-dilated patients and the normal TAPSE value in both the

normal RV and dilated RV groups indicated that RV systolic function impairment alone is not necessarily associated with high mortality. It was the presence of ACP that led to decreased TAPSE values and high mortality, suggesting that in such patients, all cardiac compensatory mechanisms had been exhausted [16].

Saga Jason et al. reported TAPSE values of less than 17mm in 20% of patients with COVID-19 infection, out of a total of 74. All patients included in this study were COVID-19 positive and admitted to the Intensive Care Unit (ICU). Within the first 72 hours of admission to the ICU, transthoracic echocardiography (TTE) was performed as part of the standard ICU protocol. Patients were stratified into groups based on the presence or absence of RV systolic dysfunction. The mean TAPSE value was calculated to be 15 in the group with systolic dysfunction (n=13), which was significantly lower than the mean TAPSE value of 20 in the COVID-19 group with normal RV function (n=45) [15].

Right Ventricular- fractional area change (RV-FAC):

Right ventricular Fractional Area Change (RV-FAC) provides insight into the overall RV systolic function. RV-FAC is calculated using the formula RVFAC = [(RVEDA - RVESA) / RVEDA] × 100 [10]. An RV-FAC value less than 35% is indicative of systolic dysfunction in the right ventricle [9].

Mahmoud-Elsayed et al. conducted a cohort study to assess RV function in COVID-19 pneumonia patients, using RV-FAC. Patients underwent transthoracic echocardiography (TTE) only if they had elevated levels of high-sensitivity Troponin I (hsTnI) greater than 14 ng/l. Among the total of 74 participants, 20 had a low RV-FAC value with a mean RV-FAC of 30%, indicating right ventricular impairment. When mortality was assessed, 28 out of 74 had died, with 7 of them experiencing right ventricular dysfunction, accounting for 25% of the deaths [11].

Stéphanie Bieber et al. studied COVID-19 patients with cardiac abnormalities using 3-dimensional echocardiography. A total of 32 patients were enrolled and divided into a myocardial injury group (n=18), with elevated levels of high-sensitivity Troponin T (hsTNT), and a group without myocardial injury (n=14) with normal hsTNT levels. Findings in the myocardial injury group included an enlarged RV and systolic dysfunction of the right ventricle with an RV-FAC of 37%, compared to 43% in the normal group. The difference between the two groups was statistically significant with a P value of 0.014. When follow-up was conducted in terms of admissions to the Intensive Care Unit (ICU), a total of 15 admissions were recorded, out of which 11 (61%) had abnormal FAC values [19].

Hasan Ali et al. also calculated the RV-FAC percentage in COVID-19 patients by dividing the total enrolled patients (n=90) into two groups: severe (n=44) and non-severe (n=46) COVID-19 patients. RV-FAC% was found to be significantly different in the two groups, with mean values of (41.4±4.1) and (45.5±4.5) in the severe and non-severe groups, respectively [8].

Systolic Pulmonary Artery Pressure (sPAP):

Bilateral lung involvement is commonly observed in COVID-19 patients, often leading to the development of pulmonary fibrosis and changes in pulmonary vasculature, ultimately resulting in pulmonary hypertension (PH). These vascular changes, in turn, affect RV function and can lead to right heart failure [20]. Recent studies have reported a 13% prevalence of PH in COVID-19 cases [20]. Transthoracic echocardiography provides a feasible and accurate means of evaluating systolic arterial pressure and RV function [17]. An sPAP value of ≥35 mm Hg is considered indicative of PH [21, 22]. The severity of cardiovascular illness in COVID-19 patients can be determined by the presence of pulmonary hypertension, which holds important prognostic significance.

Hasan Ali et al. evaluated sPAP by measuring the peak velocity of tricuspid regurgitation (TRV) in a cross-sectional study of COVID-19 patients. PH with an sPAP ≥35 mm Hg was observed in 14% of patients (6 out of a total of 46) in the non-severe group, compared to 38% (17 out of 44) of patients in the severely ill group, where severity of illness was defined by the presence of respiratory distress, oxygen saturation ≤ 93% at rest, and critical complications such as respiratory failure or the need for mechanical ventilation (MV). Linear regression analysis indicated that sPAP was an independent predictor of RV dilatation. However, the use of MV was associated with increased pulmonary arterial pressure, as described by D'Andrea et al. in their analysis of the effects of MV on pulmonary hemodynamics [8].

Omer Faruk et al. investigated RV function and PH by assessing sPAP values. They selected a total of 100 patients, dividing them into a non-severe group (n=56) and a severe group (n=44). A control group (n=45) was also included. Two-dimensional echocardiography was used. Severity of illness was defined as the

presence of respiratory distress, low oxygen saturation ≤ 93% at rest, a ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air ≤ 300 mmHg, or a critical condition such as septic shock. In the severe group, the mean sPAP value was (36.5 ± 10), compared to a mean value of (28.7 ± 6.3) in the non-severe group, showing a significant difference. A P value < 0.05 was found between the control and severe groups, as well as between the severe and non-severe groups. Mortality was calculated to be 50% (22 out of 44) in the severely ill group. However, the data did not demonstrate the role of sPAP as an independent predictor of mortality in these cases [3].

Emilio Daniel et al. evaluated cardiac function through echocardiography in a cross-sectional study of COVID-19 patients who were on mechanical ventilation. Abnormal sPAP values ≥35 mm Hg were observed in 54 out of a total of 140 patients. These 54 patients were divided into two groups: RV-dilation and right ventricular (RV) dilation + Acute Cor Pulmonale (ACP) group. sPAP values in these two groups were calculated as sPAP = 36 (IQR; 29-44) mm Hg and sPAP = 49 (IQR; 43-55) mm Hg, respectively. In the group with a normal right ventricle size (n=86), an sPAP of 32 (IQR; 28-37) was recorded, which was within normal limits [16].

TABLE:2 Echocardiographic parameters of Right ventricle, showing functional abnormalities

Functional echocardiography parameters of Right ventricle				
	TAPSE < 17mm	**Disease Outcome**		
		%Mortality*	**Hospital stay**	**Other complications**
Study#4(Yingxian Liu et al)	28% (12/43)	54.5%		
Study#15(Emilio Daniel et al)	11.4% (16/140)	70%		
Study#8(Saga Jansson et al)	20% (15/74)	11.1%		
	RV-FAC < 35%			
Study#5(Mahmoud-Elsayed et al)	27% (20/74/)	25%		
Study#7(Stéphanie Bieber et al)	56.2% (18/32)			61% (11/15) admission to ICU
	sPAP≥35mm Hg			
Study#15(Emilio Daniel et al)	38.5% (54/140)	70%		

TAPSE=Tricuspid annular plane systolic excursion, *RV-FAC* = right ventricular-fractional are change, sPAP =systolic pulmonary artery pressure, *represents %mortality calculated out of total number of deaths

CONCLUSION:

In this review, we observed that functional parameters of echocardiography are much more deteriorated in right ventricle as compared to the anatomical parameters including RVD and abnormal RVEDA/LVEDA ratio. Among the functional parameters, abnormal TAPSE was associated with higher percentages of poor disease outcomes in terms of mortality rate. Mortality was also higher in cases with abnormal sPAP. However, abnormal FAC has little association with mortality and but it showed poor prognosis in relation to increase ICU admissions. Among anatomical parameters, RVD was more commonly associated with mortality rate as compared to abnormal RVEDA/LVEDA.

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