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*Research Article*

# Bedside Transthoracic Echocardiology In Critically ill COVID-19 Patients

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**Abstract**
**Background:** Coronavirus disease 2019 (COVID-19) is a contagious respiratory disease that resulted from infection with a new coronavirus (SARS-CoV-2). The high prevelance of spread is the most critical issue about, millions of people have been infected all over the world, and hundreds of thousands of deaths had been recorded**.** Echocardiography is a commonly used noninvasive imaging tool for the assessment of cardiac pathology. Despite the limitations related to risk of performing personnel exposure, echocardiograghy can be a very useful tool for guiding management with various finding related to the cardiac COVID involvement. The aim of this study is to determine the role of transthoracic as well as speckle-tracking echocardiograghy in clinical assessement of critically ill COVID-19 patients. **Method**: A prospective study in which COVID-19 positive patients, admitted to quarantine of Minia University Hospital through the period from December 2019 to December 2020,underwent TTE initially then parameters were compared according to clinical deterioration. TTE and STE also were done to critically ill patients before and after remedesivir treatment. **Results:** Significant differences in TAPSE values were observed between group I and group II with mean± SD: 14.85 ± 3.29 and 19.35 ± 4.01, respectively. Also, significant larger basal RV diameter in critically ill patients (mean±SD: 39.93 ± 3.08) vs (mean±SD: 38.67 ± 2.82) in clinically stable patients (p value: 0.034). all TTE and STE used parameters showed highly significant improvement in RV systolic and diastolic dysfunction after treatment with remedesivir therapy. **Conclusion:** Echocardiograghy plays a crucial role in COVID-19 management. 2D TTE can be useful in predicting disease severity. Both 2D TTE and speckle tracking accurately diagnose cardiac involvement of critically ill COVID-19 patients; detect myocardial changes through course of treatment. Recovery of patients treated with antiviral remedesivir drug from severe COVID-19 illness may be accompanied with general improvement of RV systolic and diastolic dysfunction.

**Key words:** covid-19, transthoracic echocardiography.

## Introduction

Coronavirus disease 2019 (COVID-19) is a contagious respiratory disease that resulted from infection with a new coronavirus (SARS-CoV-2). The high prevelance of spread is the most critical issue about, millions of people have been infected all over the world, and hundreds of thousands of deaths had been recorded(1). COVID-19 pandemic attack reached over 45 million confirmed infections and threatened the lives of more than 1.2 million people worldwide(2). The clinical presentation of COVID-19 is diverse and ranges from asymptomatic to critical illness and even death. Severe and critical cases approximately represented 14% and 5% of laboratory-confirmed COVID-19 patients, respectively(1). Age and comorbidities of the infected population is related to the severity of the disease; the elderly are severely affected with high incidence of intensive care unit (ICU) need(3).The severity of symptoms is also related to the duration of disease, for mild cases, symptoms may last for 2 weeks while for severe cases it ranges from 3 to 6 weeks or more(4). Severe COVID-19 patients present signs of dyspnea, respiratory frequency ≥ 30/min, partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300 mmHg, blood oxygen saturation ≤ 93% and/or lung infiltrates > 50% within 24 to 48 hours[1]. Critically ill patients experience severe respiratory failure that requires mechanical ventilation, shock and other multiple organs failure requiring admission to ICU[5].

Case reports suggested that COVID-19 infection can cause a wide range of cardiac involvement that includes acute myocardial infarction, myocarditis and even takotsubo cardiomyopathy[6,7,8]. Acute left and right ventricular failure can be a direct consequence
of cardiac pathology, with the right sided failure also arising secondary to elevations in right ventricular afterload occurring due to pulmonary embolism or pneumonia[9]. Virus particles have been observed both in the myocardium and vascular endothelium in COVID-19 patients with cardiogenic shock[10].

Echocardiography is a commonly used noninvasive imaging tool for the assessment of cardiac pathology. Despite the limitations related to risk of performing personnel exposure, echocardiograghy can be a very useful tool for guiding management with various finding related to the cardiac COVID involvement. Transesophageal echocardiography (TEE) can efficiently assess deterioration in right and left cardiac function as well as the hemodynamic states. Cardiac enzymes such as high-sensitivity cardiac troponin T and N-terminal pro–B-type natriuretic peptide elevations can be used as predictors to select COVID-19 patients needing echocardiographic assessment[11].

In patients with COVID-19 infection, left ventricle (LV) global longitudinal strain, right ventricle (RV) global strain and free wall strain is commonly altered[12]. Myocardial strain can be accurately measured by speckle-tracking echocardiography, which can estimate LV global longitudinal strain (LVGLS), RV free wall strain (RVFWS) and RV global strain (RVGS)[13].

Currently, there is no treatment can act specifically against the SARS-CoV-2 agent. Based on the pathological features and variable clinical phases of COVID-19, the classes of drugs used are antiviral agents, antirheumatic drugs, low molecular weight heparins and hyperimmune immunoglobulins. The ongoing clinical trials should confirm safety and efficacy, and determine the different COVID-19 **stages** in which these treatments would produce the greatest benefit in terms of disease regression[14].

The aim of this study is to determine the role of transthoracic as well as speckle-tracking echocardiograghy in clinical assessment of critically ill COVID-19 patients.

## Subjects and Methods

### Subjects

One hundred and thirty-four patients were admitted to patient's quarantine of Minia University Hospital after having been diagnosed as COVID-19 positive depending on polymerase chain reaction 'PCR' of nasopharyngeal swabs through the period from December 2019 to December 2020. They underwent full echocardiographic assessment and laboratory investigations. 34 ones were excluded due to previous cardiovascular diseases. Consequently, 100 patients were included in the study. So, this study included 100 patients to know which laboratory and echocardiographic parameters that can predict early cardiac involvement in COVID-19.

**Inclusion criteria:**

Patients with positive swab for COVID-19
According to whether there is a need for mechanical ventilation or circulatory support or not, those patients were divided into two groups:

- Group I: 46 patients who needed mechanical ventilation or circulatory support.
- Group II: 54 patients who did not need mechanical ventilation or circulatory support.

**Exclusion criteria:**

1. Patients less than 18 years old.
2. Previously known structural heart disease
3. Known chest diseases, previous pulmonary embolism or other infarction.

### Methods

All participants in this study were subjected to transthoracic echocardiography (TTE) by a well-qualified operator who was blinded by the data of both groups. All studied patients underwent initial echocardiograghy within first 24 hours after admission.
According to the protocol of treatment in Minia University Hospital, group I critically ill patients were added antiviral remedesivir treatment upon

deterioration. All those patients who experienced clinical deterioration (group I who needed intubation or circulatory support) underwent two follow up TTE and speckle tracking echocardiograghy (STE), as follows:

- First assessment was just upon clinical deterioration before starting remedesivir.
- Second assessment was 2 weeks later.

The device used in the study was SIEMENS ACUSON SC 2000 ultrasound (Germany, Siemens) with its dedicated probe (4V1 probe).
Nine patients were excluded from the follow up phase of the study due to absence or death, so parameters of TTE and STE were compared to the available 37 patients of group I before and after remedesivir therapy. A flowchart in figure (1) shows the different phases of the study.

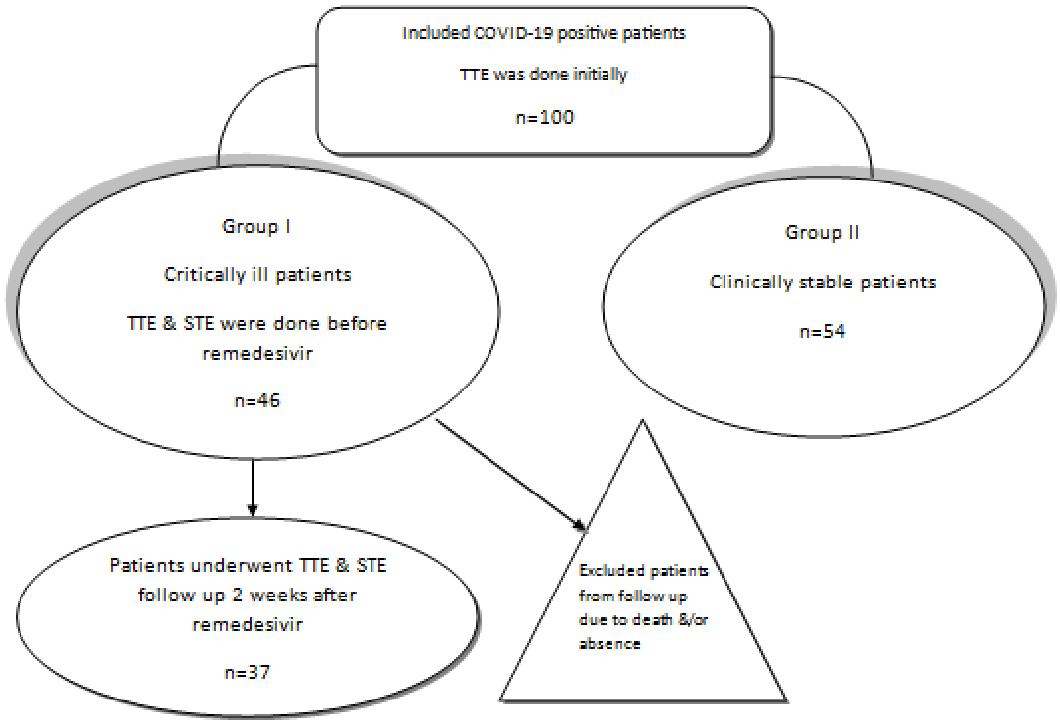


**Figure (1):** Flowchart showing different phases of the study.

○ The imaging parameters obtained by transthoracic echocardiography included:
- LV systolic function.
- LV diastolic function.
- RV systolic function by Tricuspid annular plane systolic excursion., TAPSV: Tricuspid annular plane systolic velocity .RV fractional area change, right ventricle myocardial performance index (Tei index).
- RV diastolic function using E/e`.
- Pulmonary artery systolic pressure.
- Basal RV diameter.

○ Speckle tracking transthoracic echocardiography measured parameter, RV longitudinal strain (RVLS) and systolic strain rate (SRs).

**Ethical considerations:**

- Approval of the Research Ethics Committee of the Faculty of Medicine was obtained before the study.
- Oral and written consent from the patients was obtained prior to echocardiograghy examination.
- Privacy of data was assured.

**Statistical Analysis:**

Data were checked, entered and analyzed using SPSS version 23 for data processing. The following statistical methods were used for analysis of results of the present study.
Data were expressed as number and percentage for qualitative variables and mean ± standard deviation (SD) for quantitative one.
Data were summarized using:

**Level of significance:**

For all above-mentioned statistical tests done, the threshold of significance was fixed at 5% level (*P*-value).
- *P* value of >0.05 indicates non-significant results.
- *P* value of <0.05 indicates significant results. The smaller the *P* value obtained the more significant are the results.

## Results

This study is a prospective study included patients admitted to Minia University Hospital quarantine through the period from December 2019 to December 2020. As shown in figure (1), Echocardiograghy was done for patients at several steps to evaluate its role in diagnosis and management. Included patients were divided according to their clinical course during hospital stay into 2 groups:
- **Group I:** included 46 COVID-19 patients who developed clinical deterioration; either needed mechanical ventilation or circulatory support.
- **Group II:** included 54 COVID-19 patients without clinical deterioration.

Both groups were evaluated by bedside echocardiograghy just upon admission. Table (1) shows the difference between basic Echocardiograghic parameters between groups.

**Table (1):** Differences in TTE parameters between group I and group II:

| | | Group I n= 46 | Group II n= 54 | P value |
|---|---|---|---|---|
| **TAPSE** | **Mean ± SD** | 14.85 ± 3.29 | 19.35 ± 4.01 | **0.02** |
| | **Less than 18mm** | 34 (73.9%) | 11 (20.3%) | **0.007** |
| | **More than 18mm** | 12 (26.1%) | 43 (79.7%) | |
| **Pulmonary hypertension** | **Present** | 24(52.17%) | 25(46.2) | 0.93 |
| | **Absent** | 22(47.83%) | 29(53.8) | |
| **Basal RV diameter** | **Mean ± SD** | 39.93 ± 3.08 | 38.67 ± 2.82 | **0.034*** |
| | **< 41** | 21 (45.7%) | 39 (72.2%) | **0.006*** |
| | **> 41** | 25 (54.3%) | 15 (27.8%) | |

***p value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: highly significant**
***Independent t-test**
*n: number, %: percentage, SD: Standard deviation, TAPSE: tricuspid annular plane systolic excursion, RV: right ventricle.*

Significant difference in TAPSE values were observed between group I and group II with mean± SD: 14.85 ± 3.29 and 19.35 ± 4.01, respectively. Also, significant larger basal RV diameter in critically ill patients (mean±SD: 39.93 ± 3.08) vs (mean±SD: 38.67 ± 2.82) in clinically stable patients (p value: 0.034).

Critically ill patients who needed mechanical ventilation and/or circulatory support were 46 patients. All those patients needed to receive remedsfier antiviral therapy. Echocardiograghy was done before starting therapy as well as another follow up echocardiograghy 2 weeks later. Nine patients were excluded from group I follow up due to absence or death, so parameters of TTE and STE were compared to the available 37 patients of group I before and after remedesivir therapy.

**Table (2):** Differences in TTE and STE parameters before and after remedesivir treatment of critically ill patients.

| | ECHO parameter before Remedesivir treatment mean±SD | Follow up ECHO Parameters after treatment mean±SD | P value |
|---|---|---|---|
| **TAPSE** | 13.3±3.0 | 16.7±2.4 | 0.0001 |
| **PASP (mm Hg)** | 45.4±9.7 | 37.2±7.2 | 0.0001 |
| **basal RV diameter (mm)** | 41.4±2.2 | 38.4±2.4 | 0.0001 |
| **TAPSV (cm/s)** | 9±0.6 | 9.4±0.5 | 0.002 |
| **RV MPI** | 0.44±0.07 | 0.39±0.05 | 0.001 |
| **RVFAC (%)** | 29.9±6.1 | 33.3±4.9 | 0.003 |
| **SRs (s)** | 1.01±0.19 | 0.88±0.14 | 0.004 |
| **E/e`** | 0.53±0.12 | 0.61±0.12 | 0.002 |
| **RV longitudinal strain %** | -23±4.2 | -20.3±3.3 | 0.0001 |

***p value > 0.05: Non-significant; p value < 0.05: Significant; p value < 0.01: highly significant**
***Paired samples t-test**

- *SD: Standard deviation, TAPSE: tricuspid annular plane systolic excursion, TAPSE: tricuspid annular plane systolic velocity RV: right ventricle.RVFAC: RV fractional area change. MPI : myocardial performance imaging*

Table (2) shows the difference in echocardiograghic parameters before and after antiviral treatment with remedesivir. TAPSE significantly (p value=0.0001) increased after treatment (mean±SD: 13.3±3.0 then 16.7±2.4). Pulmonary hypertension significantly improved after treatment (mean±SD: 45.4±9.7 then 37.2±7.2) (p value=0.0001). Basal RV dilatation significantly improved (p value=0.0001) after treatment (mean±SD: 41.4±2.2 then 38.4±2.4). TAPSV increased after treatment (mean±SD: 9±0.6 then 9.4±0.5) (p value=0.002). MPI was significantly (p value=0.001) higher before antiviral treatment (mean±SD: 0.44±0.07 then 0.39±0.05). RVFAC increased after antiviral therapy (mean±SD: 29.9±6.1 then 33.3±4.9) (p value=0.003). SRs decreased with antiviral therapy (mean±SD: 1.01±0.19 then 0.88±0.14) (p value=0.004). E/e` increased with antiviral therapy (mean±SD: 0.53±0.12 then 0.61±0.12) (p value=0.002). RV Speckle tracking longitudinal strain levels improved significantly with antiviral therapy (mean±SD: -23±4.2 then -20.3±3.3) (p value=0.0001).

## Discussion

COVID-19 infection, which occurs as a result of being infected with the novel coronavirus SARS-CoV-2, has established itself as a pandemic that has permeated every aspect of our lives[15]. It variously affects multiple organ systems, including the cardiovascular system. Both right ventricular and left ventricular systolic function and diastolic function can be evaluated, with right ventricular dysfunction seen most commonly in critically ill patients[16,17]. 32–55% of patients have been found to have normal transthoracic echocardiograms[16,18]. In critically ill patients, TTE can rapidly ascertain hemodynamic status and impact a patient's management[19,20]. Myocardial strain evaluation by speckle-tracking echocardiography, which can estimate left ventricle global longitudinal strain, right ventricle free wall strain and right ventricle global strain, has a diagnostic and prognostic clinical importance in several cardiac disorders[21,22,23].

The study had the aim to determine the role of echocardiograghy, whether TTE or speckle tracking, in diagnosis, prediction of severity, guiding the management and following up the clinical course of COVID-19 infection.

Our study is a prospective study in which all PCR positive COVID-19 patients admitted to Minia university hospital quarantine during the period from December 2019 to December 2020 were observed. 100 patients met the criteria of patients' selection. All included patients were further divided into two groups according to their clinical course.

Bed side echocardiograghy which was done initially upon admission was correlated with further clinical deterioration between the two groups. Significant higher TAPSE levels in clinically stable group II versus the critically ill group I (p value=0.007). Another significant difference (p value=0.006) was the more basal RV dilatation in critically ill patients when compared with the clinically stable group II (see table 1). The results points to the possible role of bedside echocardiograghy in early prediction of COVID-19 severity. This might be due to the invasive chest involvement of the evolving pandemic infection which subsequently affects the right sided heart echocardiograghic parameters.

In concordance with our results, Bursi et al.,(24) conducted echocardiograghy examination for 49 confirmed COVID-19 patients. PASP, TAPSE and RV global strain were common measured parameters used for assessment. Their results showed that Right ventricular (RV) dysfunction (as assessed by conventional and 2-dimensional speckle tracking) was a common finding and a powerful independent predictor of mortality.

In a study of Wats et al.,(25) which performed TTE to 214 patients, Primary outcome was 30-day all-cause inpatient mortality. Secondary outcomes were 30-day utilization of mechanical ventilator support, vasopressors, or renal replacement therapy. Right ventricular dysfunction, pulmonary hypertension, and moderate to severe tricuspid regurgitation were associated with increased odds for 30-day inpatient mortality. This study highlighted the importance of echocardiography and its clinical utility and prognostic value for evaluating hospitalized COVID-19 patients.

Also, in a study by Polito et al.,(26), who studied 227 COVID-19 hospitalized patients, the results showed that echocardiographic evidence of RV systolic dysfunction can be helpful in detecting COVID-19 patients at higher risk of mortality during hospitalization.
Also, in agreement with our results, El-sayed et al.,(27), study found that RV dilatation was one of the common abnormalities reported in 41% of the studied patients.

Similarly, a study by Stockenhuber et al.,(28), which compared between survivors and non survivors COVID-19 patients, reported significant difference between both groups regarding basal RV diameter.

Furthermore analysis of echocardiograghy role was done in critically ill patients of group I. More detailed TTE 2D and speckle tracking was done. Clinical deterioration of the patients required the routine addition of antiviral remedesivir treatment according to the hospital protocol. Follow up echocardiograghic examination was done two weeks later with comparing all the parameters before and after antiviral therapy. The results showed highly significant improvement of the relatively right ventricular diastolic and systolic dysfunction as well as right ventricular global strain (see table 2).

Our results suggest a lot of pathological challenges which commonly occur with this invasive contagious infection. COVID-19 infection primarily attack patients' lungs and subsequently right ventricle. Previous studies as well as our present study reported RV dysfunction in patients with acute respiratory distress syndrome and respiratory failure(29,30). Another advisable result is the highly significant improvement in RV systolic, diastolic dysfunction and strain which occurred after antiviral remedesivir therapy. This indicates the success of the treatment in improving the lung compliance and function and secondarily the RV function.

In concordance with our results, Ozer et al.,(31) was a retrospective study which compared the after recovery echocardiograghy of both home and hospital recoverd COVID-19 patients. In their study, 79 patients underwent detailed echocardiograghy recording LV end-systolic volume (LVESV), LV end-diastolic volume (LVEDV) and LV ejection fraction (LVEF) as well as TAPSE, RVFAC and SPAP. The ratio of early transmitral flow velocity (E) to late transmitral flow velocity (A) and the ratio of transmitral E to early diastolic medial septal tissue velocity (e’) was also recorded as another indicator of RV diastolic dysfunction. 42% of hospitalized patients were treated with the antiviral, favipiravir. The study demonstrated the subclinical impairment of RV function with 2D speckle tracking in hospitalized patients in relation to the severity of pneumonia after recovery. Their conclusion suggested that echocardiographers should pay close attention to the early diagnosis of RV dysfunction related to COVID-19.

Another study of Kahyaoglu et al.,[32] found that the right ventricle early inflow-outflow (RVEIO) index measured by 2D TEE can be used as a bedside, noninvasive, easily accessible, and useful marker to identify the COVID-19 patient group with widespread pneumonia and, therefore high risk of complications, morbidity, and mortality. In agreement with our results, right ventricular dysfunction was evident with severe pneumonia group but no follow up was done after recovery.

Similarily, van den Heuvel et al.,[33] compared myocardial function of hospitalized COVID-19 patients with their 4 months follow up echocardiograghy. A significantly lower RV diameter (39 vs. 34 mm, $p = 0.002$) and trend towards better global longitudinal strain (GLS) (−18.5% vs −19.1%, $p = 0.07$) was found at follow-up. However, the results were not correlated with used treatment modalities.

Another study of Lassen et al.,[34] longitudinal study found that the right ventricle was affected during acute COVID-19, but its function improved after resolution of the infection, also with no correlation with the COVID-19 treatment.

Finally, COVID-19 is a recent pandemic episode which requires more studies and investigations especially regarding different management modalities, efficacy of available antiviral therapies and their relation to myocardial function.

**Limitations:**

- The risk of infection exposure to the examiners and the burden and cost of using protective equipment were challenges faced the study work.
- Comparing the results with control healthy patients with similar risk factors would give more valuable results.

**Conclusions:**

Echocardiograghy plays a crucial role in COVID-19 management. TTE can be useful in predicting disease severity. Both TTE and STE can accurately diagnose cardiac involvement of critically ill COVID-19 patients; detect myocardial changes through course of treatment. Recovery of patients treated with antiviral remedesivir drug from severe COVID-19 illness may be accompanied with general improvement of RV systolic and diastolic dysfunction.

**Abbreviations:**

- COVID-19: Coronavirus disease 2019.
- ICU: Intensive care unit.
- STE: Speckle tracking echocardiograghy.
- TTE: Transthoracic echocardiography.
- TEE: Transesophageal echocardiograghy.
- LV: Left ventricle.
- RV: Right ventricle.
- LVGLS: LV global longitudinal strain.
- RVFWS: RV free wall strain.
- RVGS: RV global strain.
- PASP: Pulmonary artery systolic pressure.
- LVESV: LV end-systolic volume.
- LVEDV: LV end-diastolic volume.
- LVEF: LV ejection fraction.
- RV MPI: right ventricle myocardial
- performance index
- RVFAC: RV fractional area change.
- TAPSE: Tricuspid annular plane systolic excursion.
- TAPSV: Tricuspid annular plane systolic velocity.
- GLS: Global longitudinal strain.

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