

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

ECHOCARDIOGRAPHY IN COVID-19 CLINICAL INVESTIGATION

Indications for and Findings on Transthoracic Echocardiography in COVID-19

Check for updates

Sneha S. Jain, MD, MBA, Qi Liu, MD, Javant Raikhelkar, MD, Justin Fried, MD, Pierre Elias, MD, Timothy J. Poterucha, MD, Ersilia M. DeFilippis, MD, Hannah Rosenblum, MD, Elizabeth Y. Wang, MD, Bjorn Redfors, MD, Kevin Clerkin, MD, MSc, Jan M. Griffin, MD, Elaine Y. Wan, MD, Marwah Abdalla, MD, MPH, Natalie A. Bello, MD, MPH, Rebecca T. Hahn, MD, Daichi Shimbo, MD, Shepard D. Weiner, MD, Ajay J. Kirtane, MD, SM, Susheel K. Kodali, MD, Daniel Burkhoff, MD, PhD, LeRoy E. Rabbani, MD, Allan Schwartz, MD, Martin B. Leon, MD, Shunichi Homma, MD, MHCDS, Marco R. Di Tullio, MD, Gabriel Sayer, MD, Nir Uriel, MD, MSc, FACC, and D. Edmund Anstey, MD, MPH, New York, New York

Background: Despite growing evidence of cardiovascular complications associated with coronavirus disease 2019 (COVID-19), there are few data regarding the performance of transthoracic echocardiography (TTE) and the spectrum of echocardiographic findings in this disease.

Methods: A retrospective analysis was performed among adult patients admitted to a quaternary care center in New York City between March 1 and April 3, 2020. Patients were included if they underwent TTE during the hospitalization after a known positive diagnosis for COVID-19. Demographic and clinical data were obtained using chart abstraction from the electronic medical record.

Results: Of 749 patients, 72 (9.6%) underwent TTE following positive results on severe acute respiratory syndrome coronavirus-2 polymerase chain reaction testing. The most common clinical indications for TTE were concern for a major acute cardiovascular event (45.8%) and hemodynamic instability (29.2%). Although most patients had preserved biventricular function, 34.7% were found to have left ventricular ejection fractions \leq 50%, and 13.9% had at least moderately reduced right ventricular function. Four patients had wall motion abnormalities suggestive of stress-induced cardiomyopathy. Using Spearman rank correlation, there was an inverse relationship between high-sensitivity troponin T and left ventricular ejection fraction ($\rho = -0.34$, P = .006). Among 20 patients with prior echocardiograms, only two (10%) had new reductions in LVEF of >10%. Clinical management was changed in eight individuals (24.2%) in whom TTE was ordered for concern for acute major cardiovascular events and three (14.3%) in whom TTE was ordered for hemodynamic evaluation.

Conclusions: This study describes the clinical indications for use and diagnostic performance of TTE, as well as findings seen on TTE, in hospitalized patients with COVID-19. In appropriately selected patients, TTE can be an invaluable tool for guiding COVID-19 clinical management. (J Am Soc Echocardiogr 2020;33:1278-84.)

Keywords: COVID-19, Echocardiography

From the Division of Cardiology, Department of Medicine, Columbia University Irving Medical Center, New York, New York.

Dr. Clerkin receives support through National Institutes of Health (NIH) grant K23 HL148528. Dr. Abdalla receives support through grant 18AMFDP34380732 from the American Heart Association and from the NIH/National Heart, Lung, and Blood Institute (grants K23 HL141682-01A1 and R01HL146636-01A1). Dr. Bello receives support through NIH grant K23 HL136853. Dr. Poterucha owns stock in Abbott Laboratories, Abvie, Edwards Lifesciences, and Baxter International. Dr. Hahn has received speaking fees from Baylis Medical, Edwards Lifesciences, and Medtronic: has received consulting fees from Abbott Structural. Edwards Lifesciences. Medtronic, Navigate, and Philips Healthcare; has received nonfinancial support from 3mensio; holds equity in Navigate; and is the chief scientific officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she receives no direct industry compensation. Dr Kirtane reports Institutional funding to Columbia University and/or Cardiovascular Research Foundation from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, ReCor Medical.

In addition to research grants, institutional funding includes fees paid to Columbia University and/or Cardiovascular Research Foundation for speaking engagements and/or consulting; no speaking/consulting fees were personally received. Personal: Travel Expenses/Meals from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, ReCor Medical, Chiesi, OpSens, Zoll, and Regeneron. Drs. Uriel and Anstey contributed equally to this work.

Conflicts of Interest: Martin B. Leon is an advisory board participant and receives institutional grants for clinical research from Abbott, Boston Scientific, Edwards, and Medtronic. The other authors reported no actual or potential conflicts of interest.

Reprint requests: Nir Uriel, MD, MSc, FACC, Columbia University Irving Medical Center, Weill Cornell Medicine, 622 W 168th Street, PH4-129, New York, NY 10032 (E-mail: nu2126@cumc.columbia.edu).

0894-7317/\$36.00

Copyright 2020 by the American Society of Echocardiography.

https://doi.org/10.1016/j.echo.2020.06.009

Abbreviations

ASE = American Society of Echocardiography

COVID-19 = Coronavirus disease 2019

EACVI = European Association of Cardiovascular Imaging

hs-cTnT = High-sensitivity cardiac troponin T

LV = Left ventricular

LVEF = Left ventricular ejection fraction

NT-proBNP = N-terminal pro–B-type natriuretic peptide

RV = Right ventricular

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2

TR = Tricuspid regurgitation

TTE = Transthoracic echocardiography

The first case of coronavirus disease 2019 (COVID-19) was identified in Wuhan, China, in December 2019 and since has become a global pandemic, infecting 6,601,349 patients globally as of June 4, 2020.¹ COVID-19 is caused by infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).² A growing body of literature has highlighted the cardiovascular manifestations of COVID-19 and its impact on morbidity and mortality.³

Echocardiography is а commonly used noninvasive imaging tool for the assessment of cardiac pathology. However, COVID-19 places constraints on the use of echocardiography given the risk for exposure to personnel performing the study. In accordance with recommendations from the American Society of Echocardiography (ASE)⁶ and the European Association of Cardiovascular

Imaging (EACVI),⁷ our institution has limited the use of echocardiography in patients with confirmed or suspected COVID-19 to situations in which the findings are expected to provide clinical benefit. The objectives of our study were to (1) understand the clinical indications for transthoracic echocardiography (TTE) in patients with COVID-19 in the context of a global pandemic, (2) assess the feasibility and quality of transthoracic echocardiographic acquisition, and (3) and characterize the spectrum of findings on TTE in patients with COVID-19 in association with clinical assessment.

METHODS

Study Population

This study was conducted with approval from the NewYork-Presbyterian Columbia University Irving Medical Center institutional review board. Patients >18 years of age admitted to Columbia University Irving Medical Center and NewYork-Presbyterian Allen Hospital who tested positive for SARS-CoV-2 using a reverse transcriptase polymerase chain reaction assay were screened to identify if they underwent TTE during their admission from March 1, 2020, to April 3, 2020, after a positive result on SARS-CoV-2 reverse transcriptase polymerase chain reaction testing and were included in this study.

Data Collection

Data were obtained using both automated and manual chart abstraction from the electronic medical record. Abstracted data included demographics, comorbidities, presenting chief symptoms, laboratory findings, echocardiography order information, and clinical outcomes, including endotracheal intubation and death. Comorbidities were derived from documentation upon hospital admission and included the following: hypertension, diabetes, obesity (defined as body mass index \geq 30 kg/m²), coronary artery disease, pulmonary disease (including asthma, chronic obstructive pulmonary disease, interstitial lung disease, and any primary lung disease that required home oxygen therapy), stage 3 to 5 chronic kidney disease by glomerular filtration rate using the Modification of Diet in Renal Disease study equation, heart failure with a left ventricular ejection fraction (LVEF) \leq 50%, heart failure with preserved LVEF, active cancer (defined as metastatic cancer, cancer that required treatment within the past 6 months, or cancer undergoing active observation), or history of cancer that did not meet the active cancer definition. Each chart was reviewed to determine the indication for ordering TTE, and orders were grouped into one of three categories: (1) hemodynamic assessment (volume status and evaluation of shock), (2) concern for a major acute cardiovascular event (rising cardiac biomarkers, acute coronary syndrome, myocarditis, pulmonary embolism), or (3) other. Each patient chart was reviewed following TTE to assess for any changes in clinical management.

Laboratory Findings

Laboratory values of high-sensitivity cardiac troponin T (hs-cTnT) and N-terminal pro–B-type natriuretic peptide (NT-proBNP) were manually abstracted from the electronic medical, and the closest value before TTE was used for the analysis. We defined elevated hs-cTnT (>22 ng/L) and NT-proBNP (>1,800 pg/mL) by values that were greater than the 99th percentile.

Transthoracic Echocardiography

Patients underwent TTE using Affiniti and EPIQ echocardiography systems (Philips North America, Andover, MA). An abbreviated echocardiography protocol was developed using two-dimensional and Doppler imaging to limit exposure to sonographers (Supplemental Table 1). In accordance with recommendations from the ASE⁶ and EACVI,⁷ the use of echocardiography was limited in patients with confirmed or suspected COVID-19 to situations in which the findings were expected to provide clinical benefit. The clinical appropriateness of echocardiographic studies was assessed on a case-by-case basis by an attending cardiologist after chart review and discussion with the clinical care team. Sonographers were asked to follow institutional protocol surrounding personal protective equipment and ultrasound cleaning between cases and were trained in proper donning and doffing of surgical face mask, cover gowns, and eye protection including face shields or goggles.

Studies were independently analyzed by one of two board-certified echocardiographers (D.E.A. and Q.L.) who were blinded to patient data. Echocardiographic study quality was evaluated on a subjective scale of adequate, mildly limited, moderately limited, severely limited, and nondiagnostic. For an adequate-quality study, qualitative and quantitative parameters were evaluable on every image. "Mildly limited" denoted that some quantitative parameters could not be accurately assessed. In a moderately limited study, quantitative parameters were less reliable, but qualitative assessment could be performed. In a severely limited study, some qualitative parameters could not be reliably evaluated, but major parameters such as left ventricular (LV) function could still be assessed. In a nondiagnostic study, no diagnostic images could be obtained.

LV measurements were made in the parasternal long-axis views in accordance with the 2015 ASE and EACVI guidelines on chamber

HIGHLIGHTS

- TTE is performed in a minority of patients with COVID-19.
- Focused studies could be performed quickly, and the majority were diagnostic.
- Patients with elevated cardiac biomarkers more often had reduced LV function.
- In appropriately selected patients, TTE can guide COVID-19 clinical management.

quantification.⁸ Consistent with these guidelines, the normal range of LV dimensions by sex were defined as the mean \pm 1.96 SDs reported by the ASE and EACVI, and subsequent grades of abnormality (mild, moderate, and severe) were defined by incremental addition of 1 SD such that severely abnormal was a value greater than the mean + 4SDs. LVEF was assessed by visual estimation and the modified Simpson biplane method when LVEF appeared abnormal and image quality allowed accurate quantitation. Right ventricular (RV) size was assessed using RV basal and mid dimensions when technically feasible but visual estimation if image quality was not adequate for accurate measurement. RV function was assessed semiquantitatively, and valvular regurgitation was qualitatively assessed. Pulmonary artery systolic pressure was calculated on the basis of an estimate of RV systolic pressure using the tricuspid regurgitation (TR) jet⁹ and an estimate of mean right atrial pressure using the inferior vena cava size and collapsibility in nonintubated patients.¹⁰ The institutional echocardiography database was also searched for prior studies on each patient, and the most recent prior study was analyzed by one of the two study echocardiographers for direct comparison.

Clinical Outcomes

The clinical outcomes of death and mechanical ventilation were assessed by chart review for 30 days after TTE.

Statistical Analysis

Descriptive statistics only are reported for demographics, comorbidities, laboratory and echocardiographic findings, and clinical outcomes. For laboratory and echocardiographic measurements, continuous variables are expressed as mean \pm SD. Categorical variables are summarized as counts and percentages. The laboratory values of hs-cTnT and NT-proBNP were log-transformed before analyses to ensure normal distribution. Correlations between hs-cTnT and NT-proBNP and their individual correlations with LVEF were explored using Spearman rank correlation with a qualitative interpretation of the strength of the relationship.¹¹ Statistical analyses were performed using R version 4.0.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline Characteristics

During the study period, 749 patients were admitted and found to be COVID-19 positive by SARS-CoV-2 polymerase chain reaction testing during the study period. Of these patients, 72 (9.6%) underwent formal TTE following positive results on SARS-CoV-2 testing and were included in the present analysis. Baseline characteristics

Table 1 Baseline characteristics of patients with COVID-	19
undergoing TTE	

Characteristic	n (%)
Sex, male	52 (72.2)
Age, y	
18–39	10 (13.9)
40–49	7 (9.7)
50–59	16 (22.2)
60–69	20 (27.8)
70–79	13 (18.1)
≥80	6 (8.3)
Hypertension	48 (66.7)
Diabetes	31 (43.1)
Obesity (body mass index \ge 30 kg/m ²)	34 (47.2)
Asthma, COPD, or ILD	15 (20.8)
Stage 3–5 chronic kidney disease	16 (22.2)
Heart failure with reduced LVEF	15 (20.8)
Heart failure with preserved LVEF	2 (2.8)
Coronary artery disease	13 (18.1)
Active cancer	3 (4.2)
History of cancer	4 (5.6)
Orthotopic heart transplantation	5 (6.9)
LV assist device	1 (1.4)
Atrial fibrillation	2 (2.8)

COPD, Chronic obstructive pulmonary disease; ILD, interstitial lung disease.

are shown in Table 1. There were 52 men (72.2%) and 20 women (27.8%), with a median age of 61 years (interquartile range, 50.8–70.3 years). Medical comorbidities included hypertension (66.7%), diabetes (43.1%), obesity (47.2%), history of coronary artery disease (18.1%), and reduced LVEF (20.8%). Presenting symptoms included shortness of breath (70.8%), cough (61.1%), fever (59.7%), diarrhea (18.1%), and chest pain (13.9%). Forty patients (55.6%) were on mechanical ventilation at the time of TTE. The median time from admission to TTE was 3 days.

Indications for TTE

The most common clinical indications for ordering TTE included hemodynamic assessment (29.2%) and concern for a major acute cardiovascular event (rising cardiac biomarkers, pulmonary embolism, acute coronary syndrome, heart failure, or myocarditis; 45.8%). The remaining indications included known history of cardiac disease, evaluation for endocarditis, and evaluation for cardioembolic source of stroke (Figure 1).

Technical Characteristics of TTE

On average, studies were performed in 6.7 ± 3.4 min and included 39.7 ± 17.5 clips. Twenty-nine studies (40.3%) were adequate or mildly limited in quality, 29 (40.3%) were moderately limited, 10 (13.9%) were severely limited, and four (5.6%) were nondiagnostic. Among the 40 intubated patients, 12 studies (30%) were adequate or mildly limited, 16 (40%) were moderately limited, nine (22.5%) were severely limited, and three (7.5%) were nondiagnostic.

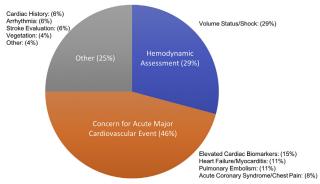


Figure 1 Indications for performing TTE in patients with COVID-19.

Echocardiographic Findings

Diastolic and systolic LV measurements could not be measured in 10 (13.9%) and 24 (33.3%) patients, respectively (Supplemental Table 2). LV diastolic and systolic linear dimensions were increased in six (8.3%) and 12 (16.7%) patients, respectively. LV global and regional function are listed in (Table 2). LVEF was evaluable in 68 patients (94.4%). Of these, 59 (87%) were assessed by visual estimation, and nine (13%) were assessed using the modified Simpson biplane method. The majority (59.7%) of the cohort had LVEFs > 50% (Table 2). Thirty-two patients (44.4%) had normal wall motion, while 17 (23.6%) had global hypokinesis or segmental wall motion abnormalities. The pattern of wall motion abnormalities was suggestive of stress-induced cardiomyopathy in four patients. The majority of patients had LV septal and posterior wall thicknesses that were normal (38.9%) or mildly thickened (36.1%; Supplemental Table 3). Patterns of LV hypertrophy are shown in Supplemental Table 4.

RV size was normal or borderline increased in 50 patients (69.4%; Table 3). Nine patients (12.5%) had mildly increased RV size, and only two patients had moderately or severely increased RV size. RV function was normal in 34 (47.2%), mildly decreased in 19 (26.4%), moderately decreased in seven (9.7%), and severely decreased in three (4.2%) patients (Table 3).

Moderate or greater valve regurgitation was noted in seven patients (one with moderate aortic insufficiency, two with moderate or severe mitral regurgitation, and four with moderate or severe TR). An accurate maximal TR velocity could be evaluated in 26 patients (36.1%), while 46 (63.9%) could not be evaluated because of poor data quality or incomplete TR envelopes. Nine patients (12.5%) had peak TR velocities > 2.8 m/sec, while 17 patients (23.6%) had peak TR velocities < 2.8 m/sec. Inferior vena cava measurements for estimation of right atrial pressure could be accurately assessed in 35 patients (48.6%). Of that sample, 24 were intubated at the time of TTE. Of 11 nonintubated patients with interpretable inferior vena cava measurements, eight had estimated right atrial pressures of 0 to 5 mm Hg, two patients had estimated right atrial pressures of 5 to 10 mm Hg, and one patient had an estimated right atrial pressure of 10 to 20 mm Hg.

The majority of participants had no (69.4%) or trace (22.2%) pericardial effusion. Small pericardial effusions were present in 4.2% (Supplemental Table 5). No patients had echocardiographic signs of cardiac tamponade. The presence of a pericardial effusion could not be assessed in three participants (4.2%).

Table 2 LV function among patients with COVID-19 undergoing TTE Image: Coving TTE

LV global and regional function	n (%)
LV function	
Normal LVEF (>50%)	43 (59.7)
Reduced LVEF (≤50%)	25 (34.7)
Unable to assess	4 (5.6)
Segmental LV wall motion	
Normal	32 (44.4)
Global hypokinesis	9 (12.5)
Segmental wall motion abnormalities	8 (11.1)
Apical hypokinesis with basal sparing	4 (5.6)
Left anterior descending coronary artery distribution	2 (2.8)
Right coronary artery distribution	1 (1.4)
Multivessel distribution	1 (1.4)
Unable to assess	23 (31.9)

 Table 3
 RV size and systolic function among patients with

 COVID-19 undergoing TTE

RV size and systolic function	n (%)
RV size	
Normal	50 (69.4)
Mildly increased	9 (12.5)
Moderately increased	2 (2.8)
Severely increased	0 (0)
Unable to assess	11 (15.3)
RV systolic function	
Normal	34 (47.2)
Mildly decreased	19 (26.4)
Moderately decreased	7 (9.7)
Severely decreased	3 (4.2)
Unable to assess	9 (12.5)

Stratified Analysis by Cardiac Biomarkers

Sixty-nine of 72 patients (95.8%) had hs-cTnT measured before TTE, and 48 patients had NT-proBNP measured before TTE (Table 4). There was a weak inverse relationship between hs-cTnT and LVEF ($\rho = -0.34$, P = .006). There was a trend toward a weak inverse relationship between NT-proBNP and LVEF ($\rho = -0.29$, P = .056), which did not meet statistical significance (Supplemental Figure 1).

Cardiac biomarkers	Normal value before TTE, n (%)	Elevated value before TTE, n (%)	Unknown, <i>n</i> (%)
hs-cTnT	(<i>n</i> = 23)	(<i>n</i> = 46)	(<i>n</i> = 3)
Normal LVEF (>50%)	16 (69.6)	24 (52.2)	3 (100)
Reduced LVEF (≤50%)	4 (17.4)	21 (45.7)	_
Unable to assess	3 (13)	1 (2.2)	_
NT-proBNP	(<i>n</i> = 27)	(<i>n</i> = 21)	(<i>n</i> = 24)
Normal LVEF (>50%)	19 (70.4)	10 (47.6)	14 (58.3)
Reduced LVEF (≤50%)	5 (18.5)	11 (52.4)	9 (37.5)
Unable to assess	3 (11.1)	0 (0)	1 (4.2)

Table 4 LVEF among patients with COVID-19, stratified by normal or elevated hs-cTnT and normal or elevated NT-proBNP before undergoing a transthroacic echocardiogram

Normal hs-cTnT was defined as \leq 22 ng/L, elevated hs-cTnT was defined as >22 ng/L, normal NT-proBNP was defined as <1,800 pg/mL, and elevated NT-proBNP was defined as \geq 1,800 pg/mL.

Comparison with Prior Echocardiograms

Twenty individuals in this cohort had prior transthoracic echocardiograms available for review. On average, the prior echocardiograms were obtained in 18 min and included 91.7 clips. On prior TTE, seven patients had reduced LVEFs of <50%, of whom all seven also had reduced LVEFs of <50% on current TTE. When comparing the previous and current echocardiograms, two patients had reductions in LVEF of >10%. Of these, one patient had a previously normal LVEF and new wall motion abnormalities consistent with stressinduced cardiomyopathy, while the other had worsened global LV function of a previously diagnosed cardiomyopathy. One patient had an increase in RV size from the prior study. Six patients had reductions in RV function, with five decreasing from normal to mildly reduced and one decreasing from mildly to moderately reduced. Three of the eight patients with focal wall motion abnormalities had prior transthoracic echocardiograms. Of those patients, two had preexisting wall motion abnormalities.

Changes in Management and Outcomes Following TTE

Abnormal findings on TTE directly affected clinician decisionmaking in 12 patients (16.7%). Clinical management was changed in eight individuals (24.2%) who underwent TTE because of concern for acute major cardiovascular event and three (14.3%) in whom TTE was ordered for hemodynamic evaluation. Four patients had findings consistent with pulmonary embolism and were started on anticoagulation. The remaining eight patients had newly discovered LV systolic dysfunction, and four were critically ill. Two patients were started on inotropic support, and one patient who was already on venovenous extracorporeal membrane oxygenation had an arterial limb added. One patient was transferred from an affiliated community hospital to the main campus for evaluation for extracorporeal membrane oxygenation; this patient was declined for extracorporeal membrane oxygenation by a multidisciplinary heart team but eventually was weaned off vasoactive agents. Three patients were diagnosed with systolic heart failure and were started on therapies or arranged to have outpatient cardiology follow-up. Finally, one patient was planned for a trial of diuresis, but given poor prognosis related to cardiomyopathy and other comorbidities, the patient was transitioned to comfort-focused care. During the 30-day follow-up period after TTE, four patients who were previously not intubated required intubation, and 24 (33.3%) died (Supplemental Table 6).

DISCUSSION

In this study, we describe the technical characteristics and cardiac findings of 72 transthoracic echocardiographic examinations performed on SARS-COV-2-positive patients at a quaternary care center in New York City. Our main findings are as follows: (1) echocardiographic examinations were performed in only a minority of patients with COVID-19, (2) sonographers spent less time and obtained fewer images than usual, (3) the majority of tests were diagnostic and were able to address the clinical question for which they were ordered, (4) patients with elevated hs-cTnT and elevated NT-proBNP were more likely to exhibit reduced LV function, and (5) a large proportion of patients had reduced RV function.

In the setting of the global COVID-19 pandemic, the use and performance of echocardiography have changed significantly, as the risk for transmission to sonographers and other providers has become an important concern. As such, our laboratory has implemented rigorous screening measures and changes to the standard echocardiography protocol consistent with a recent statement from the ASE.⁶ We found that these changes translated to a decrease in the number of images acquired per study and the total acquisition time per patient. Although many studies did have some limitations in data quality, very few studies were severely limited or nondiagnostic. Given the complexity and severity of the clinical course of hospitalized patients with COVID-19, many studies were performed in the critical care setting, where patients are often unable to cooperate with examination maneuvers and there are many physical impediments to optimal image acquisition. Despite these challenges, our experience shows that the utility of echocardiography remains high, and interpretable images could be obtained efficiently in the majority of patients.

Multiple cardiac manifestations of COVID-19 have been described in case reports, including fulminant myocarditis, acute RV dysfunction, and cardiac tamponade, but the spectrum and incidence of cardiac disease in COVID-19 has not been well elucidated.^{3,4,12} In our cohort, the majority of patients were found to have preserved biventricular systolic function. However, significant LV and RV systolic dysfunction was found in a subset of patients and must be interpreted within the clinical context of a patient with COVID-19. We do not know how many of these reduced LVEFs were preexisting and results should be interpreted with caution. Little is known about the pathologic effects of COVID-19 on the myocardium. In an analysis by Li *et al.*,¹³ patients with the phylogenetically similar severe acute respiratory syndrome coronavirus had subclinical diastolic

dysfunction without significant systolic impairment. In contrast, LV systolic dysfunction was prevalent in our cohort, raising concern for potential direct viral-mediated cardiotoxicity versus systemic inflammation leading to depression of myocardial function. Four patients also had apical hypokinesis with basal sparing consistent with stress-induced cardiomyopathy, suggesting another possible etiology for acute LV systolic dysfunction.

In our cohort, RV systolic dysfunction was more common than LV systolic dysfunction. The etiology of this RV dysfunction is unclear. Fifty-six percent of the cohort was intubated at the time of their echocardiographic examinations. RV dysfunction is a known complication of hypoxemic injury, including acute respiratory distress syndrome,¹⁴⁻¹⁷ and can be a hemodynamically significant and deleterious consequence of mechanical ventilation.18,19 Furthermore, hemodynamic instability and RV dysfunction in the context of acute respiratory distress syndrome is thought to correlate with mortality.^{17,20} However, the abnormalities in RV size and function in this critically ill population may also raise concern for pulmonary thromboembolism, which is a prevalent complication of COVID-19.21 Previous studies have linked elevated D-dimer at admission to higher mortality in patients with COVID-19,²² with multiple case reports of pulmonary emboli.²³ Klok et al.²¹ recently evaluated the thrombotic complications of 184 intensive care unit patients and found that the composite incidence of symptomatic acute pulmonary embolism, deep-vein thrombosis, ischemic stroke, myocardial infacrtion, or systemic arterial embolism in COVID-19 patients was 31%, with 25 of 31 (81%) from pulmonary embolism.

The primary reasons for ordering TTE were to better understand a patient's hemodynamics or concern for an acute cardiac event as suggested by a rise in hs-cTnT or NT-proBNP, such as pulmonary embolism, myocarditis, or myocardial infarction. Abnormal biomarkers were a common indication for TTE in our cohort. Among patients with elevated hs-cTnT, 46% were found to have reduced LVEF on TTE. Guo et al.²⁴ recently described the pattern of acute increase in both hs-cTnT and NT-proBNP in patients with impending cardiac death. Given these findings, it may be reasonable to use elevations in cardiac biomarkers such as hs-cTnT and NT-proBNP as a screening mechanism for patients more likely to have clinically meaningful abnormalities on TTE. Changes in management occurred for 12 patients (16.7%) as a direct result of findings on TTE. Most notably, anticoagulation was initiated in a small subset of patients for presumed pulmonary embolism because of the findings on TTE. We postulate that additional changes in clinical management may have been influenced by TTE, such as giving more fluid for the management of shock in a patient found to have normal LV function.

In the clinical management of hemodynamically unstable patients, many echocardiographic findings may be of high clinical utility. In our cohort, biventricular systolic function could be assessed in most patients, and severe LV or RV dysfunction was seen in some critically ill patients. Other hemodynamic parameters, which may guide clinical management, include inferior vena cava size and collapsibility, and pulmonary artery systolic pressure estimation.¹⁰ In our cohort, pulmonary artery systolic pressure could not be estimated in the majority of patients, because of poor data quality or incomplete TR envelope. This highlights one of the limitations of an abbreviated protocol, as 43 patients (59.7%) had less than mild TR, and in the absence of significant TR, more thorough imaging from multiple views is often required to obtain a complete TR envelope. Communication between echocardiographers and clinical providers becomes even more important in these patients, as protocols can be better tailored

to answer specific clinical questions. In this regard, handheld echocardiography may take on increased importance during the COVID-19 pandemic, particularly for rapid assessment of the inferior vena cava as a marker of volume status.

This study must be interpreted with the context of its limitations. First, our study may be subject to referral bias, as TTE may have been ordered in more severely ill patients, and requests were further screened by a cardiologist to exclude patients in whom TTE was not indicated.

Second, this was a retrospective case series of patients admitted to a hospital with no concurrent control group. Clinical histories were abstracted from the electronic medical record and were not collected prospectively as part of a research protocol.

Third, Although this was a multisite study, it included a modest-size cohort at two hospitals staffed by the same medicine and cardiology departments. Whether similar findings would be observed in a larger, multicenter study is an important area of future investigation.

Fourth, as described in the methods, TTE was abbreviated, in keeping with ASE and EACVI guidelines. As a result of this approach, some measures such as diastolic function and strain were not performed.

Fifth, the majority of patients did not have prior transthoracic echocardiograms, which limits the ability to determine the acuity of the observed pathologies and if they preceded the diagnosis of COVID-19.

Finally, positive end-expiratory pressure was not recorded at the time of echocardiography and therefore could not be included in this analysis. Importantly, the range of normal LV dimensions is based on the mean \pm 1.96 SDs reported by the ASE and EACVI,⁸ but the degree of abnormality is based on increasing SDs above the 95% confidence limit for the measure and may require further validation.

CONCLUSION

This study summarizes the various echocardiographic findings of hospitalized patients with COVID-19 and suggests that echocardiography may be a clinically useful tool for guiding management in appropriately selected patients. Elevated cardiac biomarkers, including hs-cTnT and NT-proBNP, may be useful tools as part of the clinical assessment to determine which patients with COVID-19 are likely to have abnormal findings on TTE.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi. org/10.1016/j.echo.2020.06.009.

REFERENCES

- 1. Dong E, Du H, Gardner L. An interactive Web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020;20:533-4.
- Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. COVID-19 in critically ill patients in the Seattle region—case series. N Engl J Med 2020;382:2012-22.
- **3.** Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, et al. COVID-19 and cardiovascular disease. Circulation 2020;141: 1648-55.

- 4. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. J Am Coll Cardiol 2020; 75:2352-71.
- Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, et al. The variety of cardiovascular presentations of COVID-19. Circulation 2020; 141:1930-6.
- Kirkpatrick JN, Grimm R, Johri AM, Kimura BJ, Kort S, Labovitz AJ, et al. Recommendations for echocardiography laboratories participating in cardiac point of care cardiac ultrasound (POCUS) and critical care echocardiography training: report from the American Society of Echocardiography. J Am Soc Echocardiogr 2020;33:409-22.e4.
- Skulstad H, Cosyns B, Popescu BA, Galderisi M, Salvo GD, Donal E, et al. COVID-19 pandemic and cardiac imaging: EACVI recommendations on precautions, indications, prioritization, and protection for patients and healthcare personnel. Eur Heart J Cardiovasc Imaging 2020;21:592-8.
- Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39.e14.
- Quinones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. J Am Soc Echocardiogr 2002;15:167-84.
- Porter TR, Shillcutt SK, Adams MS, Desjardins G, Glas KE, Olson JJ, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr 2015;28:40-56.
- Overholser BR, Sowinski KM. Biostatistics primer: part 2. Nutr Clin Pract 2008;23:76-84.
- Szekely Y, Lichter Y, Taieb P, Banai A, Hochstadt A, Merdler I, et al. The spectrum of cardiac manifestations in coronavirus disease 2019 (COVID-19)–a systematic echocardiographic study. Circulation. Available at: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA. 120.047971. Accessed June 16, 2020.

- Li SS, Cheng CW, Fu CL, Chan YH, Lee MP, Chan JW, et al. Left ventricular performance in patients with severe acute respiratory syndrome: a 30day echocardiographic follow-up study. Circulation 2003;108:1798-803.
- Zochios V, Parhar K, Tunnicliffe W, Roscoe A, Gao F. The right ventricle in ARDS. Chest 2017;152:181-93.
- Zapol WM, Kobayashi K, Snider MT, Greene R, Laver MB. Vascular obstruction causes pulmonary hypertension in severe acute respiratory failure. Chest 1977;71:306-7.
- Zapol WM, Snider MT. Pulmonary hypertension in severe acute respiratory failure. N Engl J Med 1977;296:476-80.
- Vieillard-Baron A, Naeije R, Haddad F, Bogaard HJ, Bull TM, Fletcher N, et al. Diagnostic workup, etiologies and management of acute right ventricle failure: a state-of-the-art paper. Intensive Care Med 2018;44: 774-90.
- Vignon P, Mentec H, Terre S, Gastinne H, Gueret P, Lemaire F. Diagnostic accuracy and therapeutic impact of transthoracic and transesophageal echocardiography in mechanically ventilated patients in the ICU. Chest 1994;106:1829-34.
- Vieillard-Baron A, Millington SJ, Sanfilippo F, Chew M, Diaz-Gomez J, McLean A, et al. A decade of progress in critical care echocardiography: a narrative review. Intensive Care Med 2019;45:770-88.
- Repesse X, Charron C, Vieillard-Baron A. Acute respiratory distress syndrome: the heart side of the moon. Curr Opin Crit Care 2016;22: 38-44.
- Klok FA, Kruip M, van der Meer NJM, Arbous MS, Gommers D, Kant KM, et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis. Thromb Res 2020;191:148-50.
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.
- Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia: a random association? Eur Heart J 2020; 41:1858.
- Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:811-8.