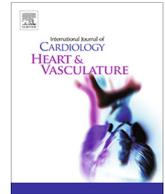




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Left ventricular global longitudinal strain in identifying subclinical myocardial dysfunction among patients hospitalized with COVID-19

Hezzy Shmueli^a, Maulin Shah^a, Joseph E. Ebinger^a, Long-Co Nguyen^a, Fernando Chernomordik^{a,b,c}, Nir Flint^{a,d}, Patrick Botting^a, Robert J. Siegel^{a,*}

^a Smidt Heart Institute, Cedars Sinai Medical Center, Los Angeles, CA, USA

^b Pulmonary and Critical Care Medicine Division, Cedars Sinai Medical Center, Los Angeles, CA, USA

^c Leviev Heart Center, Sheba Medical Center, Ramat Gan, Israel, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

^d Department of Cardiology, Tel Aviv Sourasky Medical Center, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

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ABSTRACT

Background: The incidence of acute cardiac injury in COVID-19 patients is very often subclinical and can be detected by cardiac magnetic resonance imaging. The aim of this study was to assess if subclinical myocardial dysfunction could be identified using left ventricular global longitudinal strain (LV-GLS) in patients hospitalized with COVID-19.

Methods: We performed a search of COVID-19 patients admitted to our institution from January 1st, 2020 to June 8th, 2020, which revealed 589 patients (mean age = 66 ± 18, male = 56%). All available 60 transthoracic echocardiograms (TTE) were reviewed and off-line assessment of LV-GLS was performed in 40 studies that had sufficient quality images and the views required to calculate LV-GLS. We also analyzed electrocardiograms and laboratory findings including inflammatory markers, Troponin-I, and B-type natriuretic peptide (BNP).

Results: Of 589 patients admitted with COVID-19 during our study period, 60 (10.1%) underwent TTE during hospitalization. Findings consistent with overt myocardial involvement included reduced ejection fraction (23%), wall motion abnormalities (22%), low stroke volume (82%) and increased LV wall thickness (45%). LV-GLS analysis was available for 40 patients and was abnormal in 32 patients (80%). All patients with LV dysfunction had elevated cardiac enzymes and positive inflammatory biomarkers.

Conclusions: Subclinical myocardial dysfunction as measured via reduced LV-GLS is frequent, occurring in 80% of patients hospitalized with COVID-19, while prevalent LV function parameters such as reduced EF and wall motion abnormalities were less frequent findings. The mechanism of cardiac injury in COVID-19 infection is the subject of ongoing research.

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Abbreviations: COVID-19, coronavirus disease 2019; SARS, severe acute respiratory syndrome; LV, left ventricle; TTE, transthoracic echocardiogram; LV-GLS, left ventricular global longitudinal strain; IL-6, interleukin-6; BNP, B-type natriuretic peptide; ICU, intensive care unit; CRP, C-reactive protein; LDH, lactate dehydrogenase; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; VTI, velocity-time integral; RV, right ventricle; LA, left atrium; HTN, hypertension; COPD, chronic obstructive pulmonary disease; T2DM, type-2 diabetes mellitus; TAPSE, tricuspid annular plane systolic excursion; ECG, electrocardiogram; AV, atrioventricular; CMRI, cardiac magnetic resonance imaging.

* Corresponding author at: Smidt Heart Institute, Cedars-Sinai Medical Center, 8700 Beverly Blvd, AHSP, Los Angeles, CA 90048, USA.

E-mail address: robert.siegel@cshs.org (R.J. Siegel).

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1. Introduction

The index case of coronavirus disease 2019 (COVID-19) occurred in Wuhan, China and has since rapidly expanded to a global pandemic, infecting 83,322,450 individuals and resulting in over 1,831,400 deaths in over 200 countries as of January 3rd 2021. Severe acute respiratory syndrome SARS-CoV-2 (the causative agent of COVID-19) predominantly affects the respiratory system, however multiple other organ systems, including the cardiovascular system, are involved in its pathogenesis [1,2]. Acute cardiac injury, as defined by elevation of high-sensitivity cardiac troponin-I, has been reported to range from 8 to 28% of patients with COVID-19 [3,4] and is associated with worse clinical outcomes [5–7]. Troponin-I elevation is associated with an up to a

five-fold increase in respiratory failure requiring mechanical ventilation, life-threatening arrhythmias, and mortality [8]. A variety of cardiovascular manifestations of COVID-19 have been reported, including acute myocarditis, cardiomyopathy, ventricular arrhythmias, heart failure and cardiogenic shock [9,10]. However, data regarding myocardial involvement remains scarce. A recent study found that up to 80% of patients who have recovered from COVID-19 have abnormal cardiac MRI (CMRI) findings, primarily myocardial inflammation, regional scar and pericardial enhancement [11]. These findings indicate that long-term cardiac sequela may be observed in patients without apparent myocardial involvement during acute infection. Cardiovascular involvement by COVID-19 has been determined primarily by elevated serum troponin or overt left ventricular (LV) dysfunction on transthoracic echocardiogram (TTE). However, we hypothesize that subclinical, myocardial involvement in COVID-19 may be detected as abnormal left-ventricular (LV) global longitudinal strain (GLS). LV-GLS is a sensitive marker of LV dysfunction with long-term prognostic value in many cardiac conditions, including heart failure and valvular disease [12–15]. More importantly, there is growing evidence that abnormal LV-GLS can detect myocardial injury prior to reduction in LV ejection fraction (EF) [16,17]. Since long-term complications of COVID-19 are not yet known, early identification of patients who may be at higher risk is important.

2. Materials and methods

2.1. Study design and population

In this single-center retrospective analysis, we performed a database search of all COVID-19 patients admitted to Cedars-Sinai Medical Center, Los Angeles, California between January 1st, 2020 and June 8th, 2020. We reviewed all 60 available transthoracic echocardiograms (TTE) that were performed on this group of patients. Of them, 40 studies had enough data to perform LV-GLS assessment.

2.2. Echocardiographic analysis

All TTEs were performed and analyzed in accordance with the American Society of Echocardiography (ASE) published guidelines regarding bedside focused study during the COVID-19 outbreak [18]. The studies were done on Philips Epiq-cvx machines with probe X5-1 that has 3D capability.

We performed left ventricular global longitudinal strain (LV-GLS) using speckle tracking echocardiography. Images were obtained from the apical 4-, 3- and 2-chamber views and off-line automated analysis was done using commercially available software (QLAB 13, TOMTEC/Philips Andover, MA, USA). A 17-segment polar plot (Bulls' eye) provided visual and quantitative representations of regional LV function by plotting color-coded values of peak-systolic strain [19,20]. Whenever available, the index TTE study during COVID-19 hospitalization was compared to previous studies.

2.3. General investigations

All clinical and laboratory data were extracted from electronic medical records of the study cohort. Laboratory results were obtained from the baseline values of the index hospitalization. Peak levels of inflammatory markers (D-dimer, ferritin, interleukin-6 [IL-6], lactate dehydrogenase [LDH]) were obtained as they have been shown to correlate with disease severity in COVID-19 hospitalized patients [9].

2.4. Statistical analysis

Baseline characteristics, hospital level of care and in-hospital mortality are summarized as means \pm standard deviations for continuous variables and as counts for categorical variables. Comparisons between patient groups according to TTE performance were made using the Student's *t*-test or Chi-squared test, as appropriate.

The Cedars-Sinai Institutional Review Board has approved this study protocol as it was conducted according to the declaration of Helsinki, and waived the requirement for individual written consent.

3. Results

There were 1034 positive COVID-19 cases identified at Cedars-Sinai Medical Center (mean age 56.7 ± 21.3 , male 538/1034, 52%) between January 1st, 2020 and June 8th, 2020; Of these patients, 589 were admitted to the hospital. Sixty (60/589, 10.1%) patients underwent TTE during the index hospitalization and were included in the study group. The average time between admission and the echo study was 4 ± 4 days. The most common indications for obtaining a TTE were shortness of breath (31/60, 52%) and hemodynamic instability (22/60, 36%).

Table 1 summarizes the major admission data for the entire cohort. The most prevalent comorbidities among hospitalized patients were hypertension (28/60, 46.7% in the study group) and diabetes (16/60, 26.7%). There were 195/1034 (18.9%) admissions to the intensive care unit (ICU), and 114/1034 (11%) patients requiring mechanical ventilation. Total in-hospital mortality was 87/1034, 8.4%. Among the 60 patients that underwent TTE, 35/60 (58.3%) were admitted to the ICU, 19/60 (31.7%) required mechanical ventilation and 11/60 (18.3%) patients died.

Table 2 presents the demographic, clinical, and laboratory parameters of the study group (N = 60). The most prevalent presenting symptom was dyspnea, cough as well as signs of respiratory infection (41/60, 68%). The mean hospital length of stay was 13.2 ± 9.4 days. Baseline levels of liver transaminases, creatinine, glucose, HbA1C, C-reactive protein (CRP), D-dimer, ferritin, LDH, IL-6, BNP and troponin-I levels were all elevated in this cohort.

Table 3A shows frequency of abnormal echocardiographic parameters and abnormal LV-GLS, and Table 3B shows the echocardiographic measurements and findings of the study group. The left ventricle ejection fraction (LVEF) was preserved ($\geq 50\%$) in 47/60, 78% of patients. Thirteen patients (13/60, 22%) had a reduced LVEF (mean 41.3%, range 10–50%) and larger LV end-diastolic and end-systolic diameters (4.73 ± 0.91 , $P = 0.014$ and 3.8 ± 0.99 , $P < 0.001$ respectively) compared to patients with preserved LVEF. Segmental wall motion abnormalities were common in patients with reduced LVEF, and involved various segments. Mean LV outflow tract velocity–time integral (LVOT VTI) was low ($17.7 \text{ cm} \pm 3.8 \text{ cm}$) consistent with low forward LV stroke volume (stroke volume (cc) = LVOT area (cm²) \times LVOT VTI (cm)). LV wall thickness (septal + posterior wall) was increased with no statistical difference related to wall motion abnormalities ($2.38 \text{ cm} \pm 0.84 \text{ cm}$, $P = 0.26$).

LV-GLS analysis was performed in 40/60 (67%) patients with adequate echocardiographic images for the performance of strain. As shown in Fig. 1, we found abnormal GLS in 32/40 (80%) of patients (mean LV-GLS of $-12.1\% \pm 4.0$, normal $< -16\%$). LV-GLS was significantly reduced in patients with regional wall-motion abnormalities, compared with those without regional wall motion abnormalities ($-9.7\% \pm 3.4$ and $-12.8\% \pm 4.0$ respectively, $P = 0.04$). In addition, as shown in Fig. 1, we also found bright, hyperechoic myocardium in the septal and lateral walls in 44/60 (74%) of our patient cohort. Further cases are presented in Figs. 2–3 and videos 1–8 in the Appendix to this paper.

Table 1
Baseline characteristics of patients infected with COVID-19 presenting to Cedars Sinai Medical Center between January 1st, 2020 and June 8th 2020.

	Total (N = 1034)	Not Admitted (N = 445)	Admitted with COVID-19		P-value
			No TTE (N = 529)	TTE (N = 60)	
Age, Years, mean (SD)	56.755 (21.283)	44.431 (16.967)	66.045 (19.663)	66.250 (17.128)	0.938
Male sex, n (%)	538 (52.0)	207 (46.5)	292 (55.2)	39 (65.0)	0.147
Ethnicity, n (%)					0.86
Non-Hispanic	712 (68.9)	278 (62.5)	389 (73.5)	45 (75.0)	
Hispanic	263 (25.4)	123 (27.6)	127 (24.0)	13 (21.7)	
Unknown	59 (5.7)	44 (9.9)	13 (2.5)	2 (3.3)	
Race, n (%)					0.63
White	646 (62.5)	251 (56.4)	357 (67.5)	38 (63.3)	
African American	147 (14.2)	39 (8.8)	94 (17.8)	14 (23.3)	
Asian	94 (9.1)	59 (13.3)	33 (6.2)	2 (3.3)	
Other	95 (9.2)	55 (12.4)	36 (6.8)	4 (6.7)	
Unknown	52 (5.0)	41 (9.2)	9 (1.7)	2 (3.3)	
Obesity, n (%)	157 (15.2)	59 (13.3)	88 (16.6)	10 (16.7)	0.995
Hypertension, n (%)	385 (37.2)	86 (19.3)	271 (51.2)	28 (46.7)	0.503
Diabetes mellitus, n (%)	214 (20.7)	37 (8.3)	161 (30.4)	16 (26.7)	0.546
Prior myocardial infarction or heart failure, n (%)	171 (16.5)	15 (3.4)	138 (26.1)	18 (30.0)	0.515
Prior COPD, n (%)	155 (15.0)	43 (9.7)	105 (19.8)	8 (13.3)	0.126
ICU Admission, n (%)	195 (18.9)	0 (0.0)	160 (30.2)	35 (58.3)	< 0.001
Mechanical ventilation, n (%)	114 (11.0)	0 (0.0)	95 (18.0)	19 (31.7)	0.011
In-hospital mortality, n (%)	87 (8.4)	4 (0.9)	72 (13.6)	11 (18.3)	0.319

*P value comparing patients admitted with Covid-19 who did or did not undergo a TTE.

1. Student's T-test.

2. Pearson's Chi-squared test.

TTE = transthoracic echocardiography, COPD = chronic obstructive pulmonary disease, ICU = intensive care unit.

Diastolic dysfunction (grade 2 or worse) indicative of elevated LV filling pressures was more frequent in patients with reduced LVEF compared with those with preserved LVEF (4/13, 30.8% vs. 5/47, 11.1%, $p = 0.015$).

Eleven patients (11/60, 18.3%) from the study group died during the index hospitalization, all due to shock and multi-organ failure. While 2/11, 19% of them had reduced LVEF or signs of elevated filling pressure, all of them had abnormal LV-GLS at baseline (mean $-9.9\% \pm 3.2$).

4. Discussion

Our main findings are as follows (see Tables 1–3): (1) 10.1% of patients hospitalized with COVID-19 met ASE guidelines criteria [18] for TTE evaluation based on clinical benefit due to signs or symptoms of heart failure. (2) Overt LV dysfunction, with reduced (<50%) LVEF and/or segmental wall motion abnormalities, was present in 22% of patients ($n = 13$), and diastolic dysfunction (grade 2 or worse) was present in 23%. (3) Abnormal LV-GLS was a common finding, observed in 80% of patients, with significantly worse LV-GLS values among patients with wall motion abnormalities by 2D-TTE ($-9.74\% \pm 3.42$ vs. $-12.86\% \pm 4.00$, $P = 0.04$). Although there was regional variation in abnormal LV-GLS pattern, the majority of patients (85%) had septal involvement of abnormal strain.

As GLS has been shown to be a sensitive marker of LV dysfunction, we hypothesize that LV-GLS findings may identify subclinical myocardial dysfunction in patients hospitalized with acute COVID-19 infection regardless of LV systolic function. As long-term cardiovascular complications of COVID-19 infection are yet unknown, the need for identification of high-risk patients is clinically relevant.

LV strain is a dimensionless index that describes the percent deformation between two regions of myocardium. Unlike LVEF, GLS is not limited by pathophysiologic entities that preserve the ratio of stroke volume to LV cavity size. GLS is a more sensitive marker of left ventricular dysfunction than LVEF and provides incremental prognostic value to LVEF [12,21,22]. Findings of nor-

mal LVEF and low GLS values have been reported previously in myocarditis [23–25]. Currently, the mechanism of cardiac injury in COVID-19 is uncertain. Potential etiologies may include myocarditis, systemic cytokine-mediated injury, microvascular injury or stress-related cardiomyopathy [26].

At present, myocardial injury due to COVID-19 is largely defined by elevated serum troponin levels, has a prevalence of 8–30% of affected patients, and is associated with worse clinical outcomes [27,28]. Elevated troponin levels and overt LV dysfunction on transthoracic echocardiogram (TTE) are the primary modalities for diagnosing cardiovascular complications in acute COVID-19 infection. However, a recent MRI study showed a high rate of subclinical myocardial involvement in patients with COVID-19 infection [11]. The investigators evaluated CMRI findings in 100 patients who had recovered from COVID-19 infection. In this cohort, 78% of patients were found to have myocardial involvement on CMRI in the form of myocardial inflammation, regional scar formation, or pericardial enhancement. The reported rate of myocardial injury on CMRI in this study is similar to the prevalence of abnormal LV-GLS seen in our cohort (80%). Huang et al. retrospectively studied on CMRI 26 patients who recovered from COVID-19 and had cardiac symptoms. They showed 15/26 patients (58%) had abnormal findings such as myocardial edema and late gadolinium enhancement [29]. Our findings support that a significant proportion of patients with acute or resolved COVID-19 infection may have subclinical myocardial dysfunction. This finding is significant because it may help identify patients who are at increased risk of acute as well as long-term cardiovascular complications from COVID-19 infection. While there is currently no data for long-term cardiovascular sequelae of COVID-19 infection, patients who have recovered from viral myocarditis are at increased risk for future heart failure hospitalizations [30], atrial and ventricular arrhythmias including sudden cardiac death [31], and overall decreased survival [32]. Additionally, previous studies evaluating cardiac involvement from the 2009 influenza A strain, H1N1 pandemic, found echocardiographic signs of cardiac dysfunction, such as increased left ventricular end-systolic dimension,

Table 2
Baseline characteristics and laboratory values of the study group.

n	Total
Total	
60	
Presenting Symptoms (%)	
Dyspnea/Cough	20 (37.7)
Respiratory Infection	16 (30.2)
Chest Pain	6 (11.3)
Other	18 (30)
Smoking (%)	
Never	18 (30.0)
Quit	10 (16.7)
Current	1 (1.7)
Unknown	31 (51.7)
Past Medical History (%)	
Heart Failure	8 (13.3)
Obesity	9 (15.0)
Dyslipidemia	23 (38.3)
Atrial fibrillation	4 (6.7)
Venous thromboembolism	9 (25.7)
Chronic Renal Failure	10 (16.7)
COPD	8 (13.3)
Hospital Length of Stay in Days, mean (SD)	
	13.23 (9.47)
Laboratory Values (normal range values):	
	Mean (SD)
Alkaline Phosphatase (40–150 U/L)	86.61 (46.38)
AST (5–34 U/L)	54.55 (48.56)
ALT (0–55 U/L)	40.30 (45.11)
Total Bilirubin (0.2–1.1 mg/dL)	0.83 (0.48)
Direct Bilirubin (0.0–0.5 mg/dL)	0.62 (0.57)
Indirect Bilirubin (<1.0 mg/dL)	0.47 (0.25)
Albumin (3.2–4.6 g/dL)	5.39 (10.18)
Sodium (135–145 mmol/L)	137.20 (7.13)
Potassium (3.5–5.0 mmol/L)	4.15 (0.65)
BUN (8.4–25.7 mg/dL)	31.55 (29.24)
Creatinine (0.72–1.25 mg/dL)	2.31 (3.25)
Glucose (70–99 mg/dL)	153.61 (101.72)
Hemoglobin A1C (4.5–5.8%)	7.57 (2.03)
Platelets (150–450 1000/UL)	227.68 (107.47)
PTT (22–37 SEC)	42.79 (34.14)
C-Reactive Protein (<5 mg/L)	128.65 (109.72)
D-Dimer (0.71–0.80 ug/mL FEU)	4.29 (5.21)
Ferritin (21.81–274.66 ng/mL)	2119.41 (5587.26)
Lactate Dehydrogenase (125–220 U/L)	531.71 (454.07)
IL-6 (<3.2 pg/mL)	166.78 (440.68)
BNP (<100 pg/mL)	403.13 (1018.32)
Troponin I (<0.04 ng/mL)	0.32 (0.94)
Maximum Values During Hospitalization	
	Mean (SD)
D-Dimer	6.80 (7.37)
BNP	543.96 (1141.30)
Ferritin	3049.29 (7582.28)
Troponin I	0.78 (1.84)

AST = aspartate transaminase, ALT = alanine amino-transferase, BUN = blood urea nitrogen, PTT = prothrombin time, IL-6 = interleukin 6, BNP = b-type natriuretic peptide

Table 3A
Frequency of abnormal echocardiographic parameters and abnormal LV-GLS.

Parameter	% (n/total available)
Reduced LVEF (<50%)	23% (14/60)
Reduced LVOT VTI (<20 cm)	75.6% (34/45)
Increased wall thickness (LV interventricular septum + posterior wall diameter > 2.2 cm)	56.6% (30/53)
Diastolic Dysfunction	75% (30/40)
Grade 1 Diastolic Dysfunction	52.5% (21/40)
Grade 2 Diastolic Dysfunction	17.5% (7/40)
Grade 3 Diastolic Dysfunction	5.0% (2/40)
Abnormal LV global longitudinal strain	80% (32/40)

LVEF = left ventricle ejection fraction, LVOT = left ventricle outflow tract, VTI = velocity time integral.

LV impaired relaxation and shortened ejection time [33]. Similarly, in patients with SARS infection, echocardiographic/Doppler findings of diastolic and, systolic dysfunction as well as cardiac output have been described [34].

Few studies have reported LV-GLS in the context of COVID-19 infection. In a study of 100 patients hospitalized with COVID-19, Baycan et al found that patients with acute COVID-19 infection had lower LV-GLS values, which was an independent predictor of in-hospital mortality [35]. However, the frequency of abnormal LV-GLS was not reported.

We also found that patients who died during hospitalization had lower LV-GLS values. Since standard TTE does not identify sub-clinical involvement, more advanced imaging is warranted in screening COVID-19 patients to assess prognosis and need for long-term cardiac follow up. Puntmann and Huang described that CMRI can identify patients with subclinical myocardial involvement [11,29]. However, CMRI is less available than TTE with GLS imaging for COVID-19 patients. The use of CMRI may also be problematic due financial factors and exacerbate well-known socioeconomic disparities in COVID-19 patients. Our study suggests that LV-GLS may be a viable alternative to CMRI in identifying subclinical myocardial dysfunction.

Echocardiographic features of myocarditis are generally non-specific and include global or segmental left ventricular systolic dysfunction, reduced ejection fraction, diastolic dysfunction, LV dilation, increased ventricular wall thickness as well as RV dysfunction [36]. Saricam et al. reported that focal echo-bright areas within the LV wall were observed in the 75 of 77 cases of acute myopericarditis on TTE and confirmed by CMRI to have a sensitivity was 95%; its specificity was 93%; its positive predictive value for myocarditis was 95.2% [37,38]. As shown in Fig. 1, we found segmental myocardial brightness in 74% of our study patients, and it was correlated to the abnormal segments by GLS.

Lieback et al. has validated in biopsy proven myocarditis that myocarditis causes focal increases in myocardial brightness by echocardiography [39], which has also been noted in other inflammatory disorders [37,40,41]. RV dysfunction was found in 11/58 (19%) of our patient cohort, and it was moderate to severe dysfunction in 5/58 (9%), as shown in Table 3B. RV dysfunction is a recognized complication of COVID. There are specific imaging characteristics in both COVID-related and non-COVID related myocarditis. Aquaro et al. found signs of RV involvement in 27/151 (17.8%) patients suspected for acute myocarditis that underwent CMRI. All 27 patients had RV edema at T2-STIR, as 13/27, 48%, had RV-continuous edema from LV and ventricular septum. Late gadolinium enhancement was found in 11/27 patients (41%) [42]. Li Yuman et al. followed after 120 COVID-19 patients with several RV function parameters such as RV fractional area change, TAPSE, annular systolic excursion and RV longitudinal strain. The patients in the lower tertile of these parameters had higher heart rate, inflammatory markers, respiratory complications, mechanical ventilation and mortality rate. The non-survivors in that study (18/120, 15%, after follow up of 51 days) displayed enlarged right heart chambers, diminished RV function, and elevated pulmonary artery systolic pressure. Male sex, acute respiratory distress syndrome, RV longitudinal strain, RV fractional area change and tricuspid annular plane systolic excursion were significant univariate predictors of higher risk for mortality in that study [38].

Our study had several limitations. This is a retrospective single-center observational study. In accordance with the safety recommendations of the ASE during the COVID-19 pandemic, TTE studies

Table 3B
Echocardiographic Parameters of the study group divided by wall motion abnormalities (normal range).

n	Total Mean (SD)	No Wall Motion Abnormality 47	Wall Motion Abnormality 13	P Test
Left Ventricular Ejection Fraction % (55–65%)	56.62 (12.80)	61.00 (6.97)	41.34 (17.35)	<0.001
Left Ventricular End Diastolic Diameter cm, (4.2–5.9)	4.31 (0.72)	4.17 (0.60)	4.73 (0.91)	0.014
Left Ventricular End Systolic Diameter cm, (2.3–3.9)	3.04 (0.87)	2.80 (0.68)	3.76 (0.99)	<0.001
Interventricular Septum cm + Posterior Wall Thickness cm (<2.2)	2.38 (0.84)	2.31 (0.41)	2.61 (1.53)	0.26
Right Ventricular base end-diastolic Diameter cm, (2.0–4.2)	3.52 (0.70)	3.44 (0.67)	3.75 (0.77)	0.183
LVOT VTI cm (20–30)	17.74 (3.94)	18.15 (3.94)	16.64 (3.90)	0.263
Stroke Volume, cc	54.78 (12.11)	56.75 (12.05)	50.19 (11.60)	0.178
TAPSE cm (>1.6)	2.00 (0.50)	2.09 (0.50)	1.68 (0.38)	0.027
Peak PA systolic Pressure mmHg (10–33)	30.00 (12.97)	26.53 (12.25)	40.40 (9.69)	0.034
Right Atrial Pressure mmHg (0–5)	4.57 (3.55)	3.56 (2.14)	7.56 (5.13)	0.003
Diastolic Function (%)				0.041
Normal	10 (16.7)	10 (22.2)	0 (0.0)	
Grade 1	21 (35.0)	16 (35.6)	5 (38.5)	
Grade 2	7 (11.7)	5 (11.1)	2 (15.4)	
Grade 3	2 (3.3)	0 (0.0)	2 (15.4)	
Not assessed	20 (33.3)	14 (31.1)	4 (30.8)	
LA area cm (10–19)	16.57 (4.63)	16.21 (4.30)	17.57 (5.59)	0.433
E/e lateral (<15)	9.74 (3.15)	9.24 (2.68)	11.33 (4.18)	0.129
Mitral E wave deceleration time msec (104–258)	213.53 (67.17)	219.69 (64.55)	197.27 (74.36)	0.353
GLS Endo Peak Apical 4-chamber view	–12.41% (4.71)	–13.05% (4.95)	–10.08% (2.82)	0.094
GLS Endo Peak Apical 2-chamber view	–13.02% (4.84)	–13.94% (4.78)	–9.87% (3.72)	0.024
GLS Endo Peak Apical 3-chamber view	–10.82% (3.88)	–11.26% (3.65)	–9.32% (4.51)	0.191
GLS Endo Peak Average	–12.16% (4.01)	–12.86% (4.00)	–9.74% (3.42)	0.041
RV Systolic Function (% from the entire group)				0.205
Normal	47 (81.0%)	38 (84.4%)	9 (69.2%)	
Mildly Reduced	6 (10.3%)	4 (8.9%)	2 (15.4%)	
Moderately Reduced	4 (6.9%)	3 (6.7%)	1 (7.7%)	
Severely Reduced	1 (1.7%)	0 (0%)	1 (7.7%)	

LVOT VTI = left ventricle outflow tract velocity time integral, TAPSE = tricuspid annular plane systolic excursion, PA = pulmonary artery, LA = left atrium, GLS = global longitudinal strain. P-values compare wall motion abnormalities vs no wall motion abnormalities using Student's t-test and Chi-Squared, as appropriate.

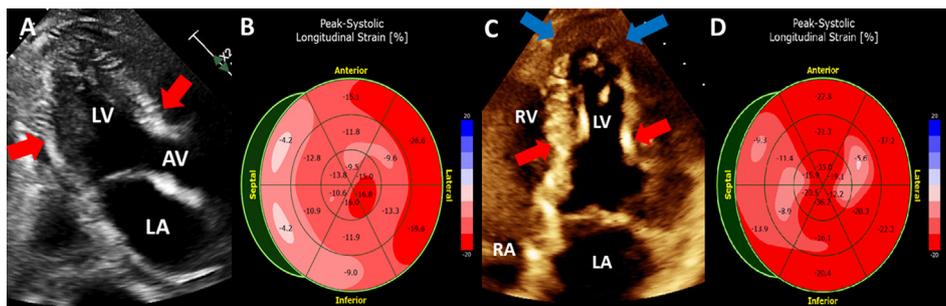


Fig. 1. A 63-year-old male, with no known medical history, presented with fever, cough and chills. After rapid respiratory deterioration correlated with high inflammatory markers and high troponin I levels, TTE was performed and showed ejection fraction (EF) of 40% with global hypokinesia, however the apical segments were relatively spared. On apical 3-chamber view (A) bright myocardium was noted at basal-septum and posterior segments (red arrows). The average peak systolic longitudinal strain “bull’s eye” imaging (B) was low –13.1 (normal values –15.9% to 22.1%), with significant dysfunction of the septal and inferior segments compared with other segments, based on numerical values and bright (less red) color. These measurements correlated with the bright segments shown in (A). After 3 weeks the patient condition significantly improved. Repeated TTE apical 4-chamber view (C) showed EF = 52% with no wall motion abnormalities. Hyperechoic bright myocardium (red arrows) was still present with relative sparing of the apical segments (blue arrows). The average peak systolic longitudinal strain “bull’s eye” imaging (D) was –19.7 (within normal limits) as the septal and inferior segments showed significant improvement. TTE = trans thoracic echocardiography, LA = left atrium, LV = left ventricle, AV = aortic valve, RA = right atrium, RV = right ventricle. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

were focused, often limited, and did not always include a comprehensive echocardiographic evaluation to permit accurate assessment of LV strain [18]. Furthermore, we could not exclude that our findings could have been present before the infection in majority of patients.

5. Conclusions

COVID-19 is a potentially lethal disease with significant cardiac complications and over 1.8 million deaths worldwide as of January 3rd 2021. Impaired LV-GLS by TTE and segmental myocardial brightness which correlated to the abnormal segments by GLS are prevalent in patients hospitalized with COVID-19. These findings are consistent with subclinical myocardial dysfunction. Addi-

tional studies are needed to better understand the prevalence of cardiac involvement in patients with COVID-19, as well as its risk factors and long-term outcomes.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcha.2021.100719>.

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