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Serial Left and Right Ventricular Strain Analysis in Patients Recovered from COVID-19

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Background: Strain analysis of transthoracic echocardiography (TTE) is a sensitive tool to detect myocardial dysfunction in those affected by COVID-19. Consideration of preexisting cardiovascular disease is important in detecting changes related to COVID-19. We sought to assess serial TTE changes in patients recovered from COVID-19 compared with baseline, pre-COVID-19 exams, with a focus on left and right ventricular longitudinal strain.

Methods: This retrospective review of serial TTEs in confirmed COVID-19 patients at Mayo Clinic sites included patients who had a TTE within 2 years prior to confirmed COVID-19 diagnosis, and the first available outpatient TTE after diagnosis was used as a comparison. Patients with interval cardiac surgery, procedure, or device placement (n = 9) were excluded. Biventricular strain was retrospectively performed on both echocardiograms.

Results: Of 259 individuals, ages 60 ± 16 years, 47% female, and 88% Caucasian, post-COVID-19 TTEs were performed a median of 55 days (interquartile range, 37-92) following diagnosis. No clinically significant TTE changes were noted, although left ventricular ejection fraction was higher (58% vs 57%, P = .049) and tricuspid annulus plane systolic excursion was lower (20 vs 21 mm, P = .046) following COVID-19. Baseline left ventricular global longitudinal strain (LV GLS) and right ventricular free wall strain (RV FWS) were normal (–19.6% and –25.8%, respectively) and similar following COVID-19 (–19.6% and –25.7%, P = .07 and .77, respectively). In the 74 inpatients, no significant change from baseline was seen for LV GLS (–19.4% vs –19.1%, P = .62), RV FWS (–25.5% vs –25.0%, P = .69), or left ventricular ejection fraction (57% vs 57%, P = .71). A significant worsening in strain occurred in 27 patients, 16 (6.8%) of the 237 with LV GLS and 14 (6.0%) of the 235 with RV FWS. Ten (20%) patients reporting new symptoms following COVID-19 had worsened strain, compared with 5 (7%) with persistent/progressive symptoms and 11 (9%) with no new symptoms (P = .04).

Conclusions: While patients with new symptoms following COVID-19 were more likely to have a worsening in absolute strain values, no clinically significant change in TTE parameters was evident in most patients following COVID-19 regardless of symptom status. (J Am Soc Echocardiogr 2022;35:1055-63.)

Keywords: COVID-19, Post-COVID-19 syndrome, Echocardiography, Strain
grams will follow abbreviated protocols and may not be ideal for strain analysis. 

In addition, hemodynamic alterations related to acute respiratory distress syndrome or use of inotropes and mechanical ventilation could impact the results of studies obtained while patients are acutely ill, particularly right ventricular free wall strain (RV FWS). Therefore, the aim of this study was to evaluate echocardiograms in patients with laboratory-confirmed COVID-19 at Mayo Clinic sites. Patients were identified through Mayo Clinic’s established registry of confirmed and recovered COVID-19 patients as of January 2021. Identified patients were then cross-referenced with the echocardiography laboratory database. Demographic and clinical information was abstracted from the medical record.

**METHODS**

**Study Design**

This is an Institutional Review Board–approved retrospective review of clinically indicated serial transthoracic echocardiography (TTE) in patients with laboratory-confirmed COVID-19 at Mayo Clinic sites. Patients were identified through Mayo Clinic’s established registry of confirmed and recovered COVID-19 patients as of January 2021. Identified patients were then cross-referenced with the echocardiography laboratory database. Demographic and clinical information was abstracted from the medical record.

**Patient Population**

Included patients had a baseline TTE or stress TTE in the 2 years prior to their confirmed COVID-19 diagnosis (since January 1, 2019). The first available outpatient TTE following COVID-19 diagnosis was utilized for comparison. All baseline and follow-up TTEs were completed between January 2019 and February 2021. Medical records were reviewed for interim cardiac events; 3 patients with cardiac surgery were excluded. An additional 6 patients were excluded due to interval cardiac intervention or device placement, which could influence changes in serial strain analysis.

**Echocardiography**

Left and right ventricular longitudinal strain assessment was retrospectively performed on both echocardiograms to assess for changes that may be attributable to the diagnosis of COVID-19. This was completed by 3 experienced research sonographers who were blinded to the aims of the study. Strain analysis was completed with TomTec software, and the echocardiography core lab protocol was followed.

A significant worsening in strain was defined as a relative increase of ≥15% from the pre-COVID-19 echocardiogram and to a value greater than −18% for LV GLS and greater than −24% for RV FWS. 

**Post-COVID-19 Symptoms**

Chart review was completed on all patients to evaluate cardiopulmonary symptom status following COVID-19 infection. Charts of outpatient medical record notes at the time of the post-COVID-19 TTE were reviewed for documentation of new or persistent/progressive cardiopulmonary symptoms compared with the patient’s pre-COVID-19 baseline. Symptoms evaluated included arrhythmia, cough, lightheadedness, edema, fatigue, chest pain, palpitations, and dyspnea. Patients were sorted into 1 of 3 categories: no symptoms, new symptoms, or persistent/progressive symptoms. Seven patients had indeterminate symptom status at the time of the post-COVID-19 TTE.

**Statistical Analysis**

Individual characteristics are presented as number (percentage) for categorical variables, mean (SD) for normally distributed continuous variables, and median (interquartile range [IQR]) for nonnormally distributed variables. Changes between measurements taken on pre- and post-COVID-19 echocardiograms were analyzed using paired t test for continuous variables that were approximately normally distributed or Wilcoxon signed-rank test for continuous variables that did not appear to be normally distributed. Categorical variables were compared between time points using McNemar’s test. Comparisons of categorical variables between independent groups such as symptom status or significant changes in strain were based on chi-square test or Fisher’s exact test. Comparison of continuous variables between independent groups was based on 2-sample t test or Wilcoxon rank-sum test. Comparison of changes between groups based on symptoms was based on analysis of variance methods. Subgroup analysis was also performed in those who were managed as inpatients for COVID-19. All analyses were performed using SAS version 9.4. Two-sided tests were used, and P < .05 was set as the level of significance.

**RESULTS**

A total of 259 individuals had both a baseline echocardiogram prior to their COVID-19 diagnosis and an outpatient echocardiogram completed after recovery from COVID-19 infection. The average age of the patients included was 60 years (SD = 16), 47% were female, and 88% were Caucasian (Table 1). Approximately two-thirds (71%) of the patients were managed for COVID-19 in the outpatient setting. There was a high prevalence of comorbidities at baseline, with hypertension (58%), congestive heart failure (31%), and cardiac arrhythmias (31%) occurring most frequently (Table 1).

Of the 74 patients that were hospitalized following COVID-19 diagnosis, 66 (89%) were admitted for symptomatic COVID-19 infection and 8 (11%) had an alternative primary admitting diagnosis. Six patients (8%) required intensive care unit level of care, 3 (4%) required mechanical ventilation, and 51 (69%) required supplemental oxygen.

The pre-COVID-19 echocardiogram was obtained a median of 220 days (IQR, 98-358) prior to laboratory-confirmed COVID-19 diagnosis. The post-COVID-19 echocardiogram occurred a median...
of 55 days (IQR, 37-92) following COVID-19 diagnosis, with a median time of 37 days (IQR, 168-429) between pre- and post-COVID-19 studies. Time to post-COVID-19 echocardiogram following diagnosis was longer for those managed as inpatients versus outpatients, with a median of 68 days (IQR, 44-115) compared to 50 days (IQR, 33-77), respectively (P < .001).

Indications for pre- and post-COVID-19 echocardiograms were evaluated based on the referral diagnoses recorded at the time of echocardiography. Compared with the pre-COVID-19 indications, there were a higher number of echocardiograms obtained for the indication of heart failure on the post-COVID-19 studies (n = 18 vs n = 31, respectively; P = .007; Figure 1). There was no significant difference in the number of studies for the indications of left ventricular function, chest pain, palpitations, dyspnea, arrhythmia, or fatigue on the post-COVID-19 echocardiograms (Figure 1).

Echocardiography Data
Overall, no clinically significant changes were seen when comparing the baseline pre-COVID-19 echocardiograms to those obtained following recovery from COVID-19 infection (Graphical Abstract, Table 2). The average left ventricular ejection fraction (LVEF) at baseline was 57% (SD = 11), and it was 58% (SD = 11) following COVID-19 infection (Table 2, P = .049). When those patients who had been hospitalized for COVID-19 were evaluated separately, no

### Table 1 Patient characteristics at the time of pre-COVID-19 echocardiogram

|                          | Total (N = 259) | Significant worsening in LV GLS or RV FWS (n = 27) | No significant change in LV GLS or RV FWS (n = 225) | P value |
|--------------------------|----------------|---------------------------------------------------|---------------------------------------------------|---------|
| Age, years, mean (SD)    | 60 (16)        | 64 (15)                                           | 60 (16)                                           | .26     |
| Gender, female, n (%)    | 122 (47)       | 16 (59)                                           | 101 (45)                                          | .16     |
| Body mass index, mean (SD)| 30 (7)         | 30 (7)                                            | 30 (9)                                            | .62     |
| Race, n (%):             |                |                                                   |                                                   | .32     |
| White                    | 227 (88)       | 22 (81)                                           | 200 (89)                                          |         |
| African American         | 18 (7)         | 3 (11)                                            | 14 (6)                                            |         |
| Native American          | 4 (2)          | 0 (0)                                             | 3 (1)                                             |         |
| Asian                    | 2 (1)          | 1 (4)                                             | 1 (0.4)                                           |         |
| Other                    | 6 (2)          | 1 (4)                                             | 7 (3)                                             |         |
| Hispanic ethnicity, n (%)| 12 (5)         | 1 (4)                                             | 11 (5)                                            | .78     |
| COVID-19 management, n (%)|              |                                                   |                                                   | .07     |
| Inpatient                | 74 (29)        | 12 (44)                                           | 61 (27)                                           |         |
| Outpatient               | 185 (71)       | 15 (56)                                           | 164 (73)                                          |         |
| Comorbidities, n (%):    |                |                                                   |                                                   |         |
| Hypertension             | 150 (58)       | 18 (67)                                           | 129 (57)                                          | .36     |
| Cardiac arrhythmias      | 79 (31)        | 13 (48)                                           | 65 (29)                                           | .04     |
| Congestive heart failure | 81 (31)        | 15 (56)                                           | 60 (27)                                           | .002    |
| Coronary artery disease  | 60 (23)        | 4 (15)                                            | 53 (24)                                           | .30     |
| Cardiac amyloidosis      | 2 (1)          | 0 (0)                                             | 2 (1)                                             | >.99    |
| Cardiac transplant       | 16 (6)         | 2 (7)                                             | 13 (6)                                            | .74     |
| Diabetes mellitus        | 74 (29)        | 7 (26)                                            | 66 (29)                                           | .73     |
| Chronic kidney disease   | 47 (18)        | 6 (22)                                            | 39 (17)                                           | .55     |
| Dialysis                 | 15 (6)         | 2 (7)                                             | 13 (6)                                            | .74     |
| Other organ transplant   | 17 (7)         | 3 (11)                                            | 14 (6)                                            | .35     |
| Stroke                   | 20 (8)         | 4 (15)                                            | 16 (7)                                            | .17     |
| Chronic obstructive pulmonary disease or asthma | 51 (20) | 8 (30) | 41 (18) | .16 |
| Pulmonary circulation disorder | 12 (5) | 1 (4) | 11 (5) | >.99 |
| Chronic liver disease    | 18 (7)         | 0 (0)                                             | 18 (8)                                            | .23     |
| Cancer                   | 75 (29)        | 10 (37)                                           | 63 (28)                                           | .34     |
| Current/former smoker    | 89 (34)        | 9 (33)                                            | 77 (34)                                           | .94     |
significant change was seen between the 2 studies (57% vs 57%, P = .71). There was no significant change in left ventricular size (P = .26) or regional wall motion abnormalities (P = .76). There was no significant change in overall right ventricular size (P = .99) or global systolic function (P = .08) compared to baseline. Right ventricular systolic pressure (RVSP) was not significantly different between the 2 studies (P = .81). As for other markers of RV systolic function, a smaller portion of individuals had tricuspid annulus plane systolic excursion (TAPSE) and RV s' reported on both studies (n = 50 and 69, respectively). There was no significant change in RV s' (P = .65); however, TAPSE was higher prior to COVID-19 infection (21 vs 20, P = .046; Table 2).

Serial Left and Right Ventricular Strain Analysis

Left and right ventricular longitudinal strain was retrospectively analyzed in 237 (92%) and 235 (91%) of the included patients, respectively. LV GLS could not be measured in 15 (6%), RV FWS could not be measured in 17 (7%), and neither LV GLS nor RV FWS could be analyzed in 7 (3%) patients. Reasons for the inability to obtain strain analysis included poor image quality, contrast use, or incomplete acquisition of necessary views at the time of study completion. Prior to infection, mean LV GLS was normal at –19.6% (SD = 3.4). After COVID-19 infection, there was no significant change in the mean LV GLS (–19.6%, P = .07; Table 2). COVID-19 patients hospitalized following their diagnosis demonstrated no difference in LV GLS between pre- and post-COVID-19 echocardiograms (LV GLS, –19.4% vs –19.1%, respectively, P = .62; Table 2). Similarly, RV FWS was normal in all patients at the time of the pre-COVID-19 TTE (–25.8%) with no significant change following recovery from COVID-19 infection (–25.7%, P = .77; Table 2). Again, there was no difference comparing pre- and post-COVID-19 RV FWS in those patients who were hospitalized following their diagnosis (–25.5% vs –25.0%, P = .69; Table 2).

However, a clinically significant worsening in strain, defined as a relative increase of ≥15% from the pre-COVID-19 echocardiogram and to a value greater than –18% for LV GLS and greater than –24% for RV FWS, was seen in 27 patients including 16 (6.8%) of the 237 patients with LV GLS and 14 (6%) of the 235 patients with RV FWS. Three patients had a significant worsening in both LV GLS and RV FWS. In the 16 patients with worsened LV GLS, pre-COVID-19 mean LV GLS was –19.9% (SD = 1.7), and post-COVID-19 it was –14.5% (SD = 1.9). In the 14 patients with worsened RV FWS, results were –27.1% (SD = 3.1) before and –18.6% (SD = 4.0) after COVID-19. Compared with those with no significant change in LV GLS or RV FWS (n = 225), those with a significant worsening in strain (n = 27) were more likely to have cardiac arrhythmias (P = .04) or heart failure (P = .002) at baseline (Table 1).
Table 2  Comparison of Pre-COVID-19 and post-COVID-19 echocardiographic characteristics

| Measure                                                                 | Pre-COVID-19 echocardiogram (N = 259) | Post-COVID-19 echocardiogram (N = 259) | Data available, N | Change mean (SD) | P value |
|------------------------------------------------------------------------|---------------------------------------|----------------------------------------|-------------------|------------------|---------|
| Heart rate, beats/min, mean (SD)                                       | 73 (14)                               | 72 (13)                                | 256               | -0.2 (14.8)      | .92     |
| Atrial fibrillation/flutter, n (%)                                     | 22 (9)                                | 20 (8)                                 | 240               | .37              |         |
| Systolic blood pressure, mm Hg, mean (SD)                             | 130 (20)                              | 132 (22)                               | 257               | 1.0 (21.1)       | .76     |
| Diastolic blood pressure, mm Hg, mean (SD)                            | 74 (13)                               | 75 (12)                                | 257               | 0.6 (12.6)       | .84     |
| LV GLS, %, mean (SD)                                                  | -19.6 (3.4)                           | -19.6 (3.6)                            | 237               | -0.1 (2.5)       | .07     |
| Managed as inpatient (n = 74), mean (SD)                              | -19.4 (3.0)                           | -19.1 (3.6)                            | 70                | 0.2 (2.8)        | .62     |
| RV FWS, %, mean (SD)                                                  | -25.8 (4.5)                           | -25.7 (4.1)                            | 235               | 0.01 (4.0)       | .77     |
| Managed as inpatient (n = 74), mean (SD)                              | -25.5 (4.6)                           | -25.0 (4.6)                            | 65                | 0.2 (4.7)        | .69     |
| LVEF, %, mean (SD)                                                    | 57 (11)                               | 58 (11)                                | 259               | 1.0 (7.7)        | .049    |
| Managed as inpatient (n = 74), mean (SD)                              | 57 (12)                               | 57 (12)                                | 74                | -0.4 (8.2)       | .71     |
| LV stroke volume index, mL/m², mean (SD)                              | 44 (11)                               | 45 (12)                                | 183               | 0.5 (9.7)        | .46     |
| RWMSI, mean (SD)                                                      | 1.1 (0.3)                             | 1.1 (0.3)                              | 265               | 0.01 (0.17)      | .49     |
| RWMSI >1, n (%)                                                       | 35 (14)                               | 36 (14)                                | 259               | .76              |         |
| LV size, n (%):                                                       | 212 (83)                              | 207 (81)                               |                   |                  |         |
| Normal                                                                | 21 (9)                                | 26 (10)                                |                   |                  |         |
| Moderately enlarged                                                   | 13 (5)                                | 14 (5)                                 |                   |                  |         |
| Severely enlarged                                                     | 8 (3)                                 | 9 (4)                                  |                   |                  |         |
| LV end-diastolic dimension, mm, mean (SD)                             | 50 (7)                                | 50 (7)                                 | 239               | -0.2 (5.2)       | .63     |
| LV end-systolic dimension, mm, mean (SD)                              | 34 (8)                                | 33 (8)                                 | 219               | -0.3 (4.8)       | .36     |
| LV end-diastolic volume, mL, mean (SD)                                | 128 (56)                              | 130 (60)                               | 83                | -3.2 (29.0)      | .32     |
| LV end-systolic volume, mL, mean (SD)                                 | 60 (44)                               | 59 (45)                                | 83                | -3.1 (20.8)      | .18     |
| Septal wall thickness, mm, mean (SD)                                  | 11 (2)                                | 11 (2)                                 | 212               | 0.01 (1.7)       | .85     |
| Posterior wall thickness, mm, mean (SD)                               | 10 (2)                                | 10 (2)                                 | 212               | -0.08 (1.8)      | .78     |
| Relative wall thickness, mean (SD)                                    | 0.41 (0.09)                           | 0.42 (0.09)                            | 212               | -0.001 (0.09)    | .83     |
| Diastolic function grade:                                             |                                       |                                       |                   |                  | .53     |
| Normal                                                                | 46 (30)                               | 32 (27)                                |                   |                  |         |
| Grade 1                                                                | 34 (22)                               | 16 (13)                                |                   |                  |         |
| Grade 2                                                                | 14 (9)                                | 10 (8)                                 |                   |                  |         |
| Grade 3                                                                | 1 (1)                                 | 2 (2)                                  |                   |                  |         |
| Indeterminate                                                         | 58 (38)                               | 59 (50)                                |                   |                  |         |
| Mitral E/A ratio, mean (SD)                                           | 1.2 (0.7)                             | 1.3 (0.8)                              | 170               | -0.05 (0.69)     | .67     |
| Mitral annulus e’ medial, m/sec, mean (SD)                            | 0.07 (0.03)                           | 0.07 (0.03)                            | 183               | 0.0009 (0.02)    | .50     |
| Mitral E/e’ (medial), mean (SD)                                       | 12.4 (6.9)                            | 12.1 (6.2)                             | 179               | -0.2 (4.6)       | .52     |
| Left atrial volume index, mL/m², mean (SD)                            | 35 (13)                               | 35 (12)                                | 129               | -0.6 (8.4)       | .43     |
| Mitral valve regurgitation, moderate or greater, n (%)                | 14 (6)                                | 13 (6)                                 | 211               | .71              |         |
| Tricuspid valve regurgitation, moderate or greater, n (%)             | 14 (6)                                | 18 (7)                                 | 227               | .48              |         |
| Aortic valve regurgitation, moderate or greater, n (%)                | 5 (2)                                 | 7 (3)                                  | 191               | .16              |         |
| RV size, n (%):                                                       | 241                                   |                                        |                   |                  |         |
| Normal                                                                | 202 (82)                              | 209 (83)                               |                   |                  | .99     |
| Mildly enlarged                                                       | 35 (14)                               | 33 (13)                                |                   |                  |         |
| Moderately enlarged                                                   | 7 (3)                                 | 8 (3)                                  |                   |                  |         |
| Severely enlarged                                                     | 2 (1)                                 | 1 (0.4)                                |                   |                  |         |
| RV function, n (%):                                                   |                                       | 241                                   |                   |                  | .08     |
| Normal                                                                | 207 (83)                              | 215 (85)                               |                   |                  |         |

(Continued)
Excluding the 7 patients with neither LV GLS nor RV FWS measurements available, patients were evaluated according to post-COVID-19 symptom status and change in strain (Graphical Abstract). Of the 49 patients with new symptoms following COVID-19, a significant worsening in LV GLS or RV FWS was present in 10 (20%). Patients with new symptoms following COVID-19 infection were more likely to have a clinically significant worsening in strain (20%) compared with those who had a clinically significant worsening but with persistent/progressive symptoms (7%) or no symptoms (9%, \( P = .04 \); Graphical Abstract).

DISCUSSION

To our knowledge, this is the first study that evaluates echocardiographic changes related to COVID-19 infection by comparing baseline, pre-COVID-19 echocardiograms to those obtained following COVID-19 infection, thereby accounting for preexisting cardiovascular disease as well as abnormalities that might have been due to hemodynamic perturbations related to acute COVID illness. In this retrospective study of 259 comorbid individuals managed either as inpatients or outpatients for their COVID-19 infection, no clinically significant differences were identified comparing pre- and post-COVID-19 echocardiograms. There was no difference in overall LV GLS and RV FWS between pre- and post-COVID-19 echocardiograms, even when those who were hospitalized following diagnosis were evaluated separately. However, a significant worsening in LV GLS and/or RV FWS occurred in a small portion of individuals (6.8% and 6.0%, respectively), and those reporting new cardiopulmonary symptoms following COVID-19 infection were more likely to have a clinically significant worsening in LV GLS and/or RV FWS.

As it was recognized that myocardial injury was common in acute COVID-19 infection with many potential cardiac manifestations,1 TTE was readily poised to be the ideal diagnostic tool to help identify cardiac involvement and risk stratify patients. It was noted early on that both right and left ventricular strain were commonly abnormal in patients hospitalized with acute COVID-19 infection and were associated with increased COVID-19 mortality.4,5,24,25 However, in

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\begin{array}{lllcccc}
\text{Mildly reduced} & 32 (13) & 29 (12) & 8 (3) & 7 (3) & 6 (3) & 6 (3) & 193 & -0.2 (3.0) & .39 \\
\text{Moderately reduced} & 8 (3) & 7 (3) & 33 (11) & 33 (12) & 147 & -0.2 (10.0) & .81 \\
\text{Right atrial pressure, mm Hg, mean (SD)} & 21 (5) & 20 (5) & 69 & -1.3 (4.6) & .046 \\
\text{RV s', m/sec, mean (SD)} & 0.12 (0.03) & 0.12 (0.03) & 20 (8) & 17 (7) & 250 & .53 \\
\text{Pericardial effusion, n (%)} & 0.12 (0.03) & 0.12 (0.03) & 69 & -0.002 (0.03) & .65 \\
\text{LV}, \text{Left ventricular; RV, right ventricular; RWMSI, regional wall motion score index.}
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acute illness COVID-19 patients who can have advanced pulmonary involvement. Abnormalities of cardiac function are often a reflection of the cardiac response to the stress and treatment (i.e., inotropes, mechanical ventilation) of a systemic inflammatory illness. Furthermore, we have previously shown that many of the cardiac abnormalities observed in patients with acute COVID-19 infection were preexisting.

As the population of patients recovered from COVID-19 continues to grow, multiple publications have reported on echocardiographic findings following COVID-19 infection. Ozer et al. reported ongoing evidence of cardiac dysfunction based on abnormal LV GLS values in 1/3 of patients recovered from COVID-19 infection; however, there was no comparison to baseline or inpatient echocardiographic data. Lassen et al. found that right ventricular function measured by right ventricular longitudinal strain and TAPSE improved with recovery from COVID-19; however, LV GLS remained reduced at 3 months post-COVID-19 diagnosis. This study also demonstrated that right and left ventricular strain in those recovered from COVID-19 were lower when compared with COVID-19-free matched controls. Several other studies have compared inpatient echocardiographic findings at the time of COVID-19 infection to subsequent outpatient follow-up ranging from 1 to 4 months. The World Alliance Societies of Echocardiography COVID follow-up study, which included 153 paired baseline and follow-up echocardiograms, found no significant change in left or right ventricular function during recovery from COVID-19. However, when evaluated separately, those with impaired left or right ventricular function tended to improve. Other studies similarly suggest there is an overall trend toward improvement in biventricular function, with some studies noting concern for residual subclinical ventricular dysfunction based on strain analysis.

The current study is novel as it provides a comparison of outpatient post-COVID-19 echocardiograms to baseline pre-COVID-19 studies, thereby accounting for preexisting cardiovascular disease and avoiding acute and temporary imaging abnormalities and abbreviated examination protocols that are often followed in acute COVID-19 illness. Many echocardiographic parameters were evaluated in this population of patients recovered from COVID-19 infection, and no clinically significant differences were seen. These findings are additive to the current literature that has demonstrated there is improvement in many echocardiographic parameters following acute COVID-19 infection, further suggesting that when baseline cardiac function is taken into consideration, many patients will not experience a significant change in their cardiac structure or function due

### Table 3: Changes in TTE parameters by post COVID symptom status

| Echocardiogram:                  | No symptoms (N = 133) | Persistent/progressive symptoms (n = 70) | New symptoms (n = 49) | P value* |
|----------------------------------|-----------------------|-------------------------------------------|-----------------------|----------|
| Heart rate, beats/min, mean (SD) | -1.4 (12.2)           | -0.6 (17.4)                               | 2.2 (17.2)            | .36      |
| Systolic blood pressure, mm Hg, mean (SD) | -0.7 (20.1)           | 5.4 (22.7)                               | -2.4 (18.0)           | .09      |
| Diastolic blood pressure, mm Hg, mean (SD) | 0.9 (13.0)           | 1.2 (12.5)                               | -0.8 (11.2)           | .66      |
| LV GLS, %, mean (SD)             | -0.4 (2.1)           | -0.1 (2.4)                               | 0.4 (3.3)             | .20      |
| Managed as inpatient (n = 69), mean (SD) | 0.1 (3.1)           | 0.6 (2.0)                               | 0.1 (3.5)            | .63      |
| RV FWS (%), mean (SD)            | 0.01 (3.7)           | -0.5 (4.0)                               | 0.7 (4.5)             | .24      |
| Managed as inpatient (n = 64), mean (SD) | 0.4 (3.7)           | -1.0 (4.7)                               | 1.4 (5.8)            | .26      |
| LVEF, %, mean (SD)               | 1.3 (7.6)           | 1.4 (7.0)                               | -1.1 (8.8)           | .15      |
| Managed as inpatient (n = 73), mean (SD) | -0.2 (8.6)           | 1.2 (7.1)                               | -2.6 (8.8)            | .30      |
| LV stroke volume index, mL/m², mean (SD) | 1.8 (9.7)           | -1.5 (9.9)                               | 0.2 (9.7)            | .13      |
| RWMSL, mean (SD)                 | -0.002 (0.18)        | 0.02 (0.20)                              | 0.02 (0.08)           | .62      |
| LV end-diastolic dimension, mm, mean (SD) | -0.1 (4.9)           | -0.9 (6.1)                               | 0.6 (4.7)             | .30      |
| LV end-systolic dimension, mm, mean (SD) | -0.3 (5.0)           | -1.1 (3.7)                               | 0.7 (5.6)             | .20      |
| LV end-diastolic volume, mL, mean (SD) | -1.6 (34.6)          | -1.5 (23.6)                              | -8.5 (20.2)           | .69      |
| LV end-systolic volume, mL, mean (SD) | -5.6 (23.7)          | -0.7 (20.1)                              | 0.5 (12.8)            | .51      |
| Septal wall thickness, mm, mean (SD) | -0.1 (1.6)           | 0.5 (2.0)                               | -0.2 (1.6)            | .07      |
| Posterior wall thickness, mm, mean (SD) | -0.07 (1.8)          | 0.07 (1.9)                              | -0.15 (1.6)           | .82      |
| Relative wall thickness, mean (SD) | -0.001 (0.09)        | 0.01 (0.11)                              | -0.01 (0.08)          | .60      |
| Mitral E/A ratio, mean (SD)       | -0.11 (0.77)         | -0.02 (0.67)                             | 0.06 (0.42)           | .47      |
| Mitral annulus e’ medial, m/sec, mean (SD) | 0.002 (0.02)         | -0.001 (0.02)                            | -0.001 (0.02)         | .52      |
| Mitral E/e’ (medial), mean (SD)   | -0.9 (4.8)           | 0.4 (4.1)                               | 0.9 (4.4)             | .07      |
| Left atrial volume index, mL/m², mean (SD) | -1.6 (8.3)           | 1.1 (9.2)                               | -1.0 (7.1)           | .30      |
| Right atrial pressure, mm Hg, mean (SD) | -0.5 (3.0)           | -0.4 (3.1)                              | 0.4 (2.6)             | .30      |
| RVSP, mm Hg, mean (SD)            | -0.9 (8.6)           | -1.4 (10.7)                              | 3.8 (12.6)            | .11      |
| TAPSE, mm, mean (SD)              | -0.9 (5.7)           | -1.2 (3.1)                              | -2.0 (4.5)           | .87      |
| RV s’, m/sec, mean (SD)           | 0.004 (0.03)         | -0.01 (0.03)                             | -0.004 (0.02)         | .28      |

*Analysis of variance P value reported for comparison across 3 groups.

**LV**, Left ventricular; **RV**, right ventricular; **RWMSI**, regional wall motion score index.
to COVID-19 infection, even when assessed by a sensitive parameter such as strain.

However, we were able to identify a small portion of individuals that did experience a significant worsening in LV GLS and/or RV FWS following COVID-19 infection. These individuals were more likely to have cardiovascular comorbidities including cardiac arrhythmias and heart failure at baseline, which may contribute to a substrate for a change in strain with COVID-19 infection as preexisting cardiovascular disease has been associated with increased severity of illness.26

Notably, a large portion of the studied patients did have a milder COVID-19 illness, with many managed as outpatients and with only a few of the inpatients requiring intensive care unit care and/or mechanical ventilation. However, this mirrors what is seen in clinical practice and represents findings from a true sample of recovered COVID-19 patients. Importantly, anyone with a history of COVID-19 may experience persistent cardiopulmonary symptoms following COVID-19 infection despite the severity of their illness, often termed long COVID or post-COVID syndrome.27,28 In our studied population, there was no increase in post-COVID-19 symptom-related indications for TTE such as chest pain, dyspnea, palpitations, and fatigue. However, further chart review was completed on all patients for cardiopulmonary symptom status following COVID-19 infection, which indeed showed 19% of patients reported new and 28% reported persistent/progressive symptoms from their pre-COVID-19 baseline at the time of their post-COVID-19 TTE.

Given the potential significant clinical impact of a large number of recovered patients with post-COVID syndrome, we sought to find any associations between post-COVID-19 symptom status and echocardiographic parameters. We saw no significant differences in the change of TTE findings between those reporting new symptoms, persistent/progressive symptoms, or no symptoms from baseline following COVID-19 infection. Interestingly, when LV GLS and RV FWS changes were evaluated in the context of post-COVID-19 symptoms, patients reporting new symptoms following COVID-19 were found to be more likely to have a clinically significant worsening in absolute LV GLS and/or RV FWS values compared with those with either persistent/progressive symptoms or no symptoms. Recently published expert consensus pathways recommend a basic cardiac evaluation, including TTE, for those with cardiopulmonary post-COVID-19 symptoms,29 particularly if they are new. The current study findings indicate that left and right ventricular strain assessment should be considered as part of a comprehensive TTE in those with post-COVID syndrome, as new strain abnormalities may indicate a need for further cardiac evaluation and/or follow-up.

Limitations

This study has limitations that should be acknowledged in the interpretation of the data. The goal of this study was to evaluate for echocardiographic changes pre- and post-COVID-19 infection. However, we did not track medication use or medication changes for this study, which may have influenced echocardiographic findings. In addition, the large portion of mild COVID-19 cases may limit our ability to see differences in studied parameters. Given the retrospective nature of the study, chart review and abstraction were completed for all patients, and we excluded those known to have interval cardiac surgery or invasive cardiac procedures, but it remains possible that some patients could have had interim events performed elsewhere that were not recognized. The generalizability of the findings is limited by the fact that only surviving patients were eligible for inclusion in this retrospective review and that the population studied was largely Caucasian. Lastly, patients categorized as having persistent/progressive symptoms could indeed have delayed symptoms related to COVID-19 infection contributing to their post-COVID-19 symptom status; however, this is difficult to discern by chart review, so they are categorized separately from those with new symptoms from baseline for the purposes of this manuscript.

CONCLUSION

In this retrospective review of patients with both pre- and post-COVID-19 echocardiographic evaluation, no clinically significant change in TTE parameters was evident in most patients following COVID-19, even as detected by sensitive parameters such as strain analysis. However, patients reporting new symptoms following COVID-19 infection were more likely to have a clinically significant worsening in absolute values of LV GLS and/or RV FWS and warrant cardiac evaluation.

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REFERENCES

1. Giustino G, Pinney SP, Lala A, Reddy VY, Johnston-Cox HA, Mechanick JL, et al. Coronavirus and cardiovascular disease, myocardial injury, and arrhythmia: JACC Focus Seminar. J Am Coll Cardiol 2020; 76:2011-23.
2. Kim J, Volodarskiy A, Sultana R, Pollie MP, Yum B, Nambiars L, et al. Prognostic utility of right ventricular remodeling over conventional risk stratification in patients with COVID-19. J Am Coll Cardiol 2020;76:1965-77.
3. Pellikka PA, Naqvi TZ. The right ventricle: a target in COVID-19 cardiac insult. J Am Coll Cardiol 2020;76:1978-81.
4. Lassen MCH, Skaanup KG, Lind JN, Alhakak AS, Sengelow M, Nielsen AB, et al. Echocardiographic abnormalities and predictors of mortality in hospitalized COVID-19 patients: the ECHOVID-19 study. ESC Heart Fail 2020;7:4189-97.
5. Li Y, Li H, Zhu S, Xie Y, Wang B, He L, et al. Prognostic value of right ventricular longitudinal strain in patients with COVID-19. JACC Cardiovasc Imaging 2020;13:2287-99.
6. Krishna H, Ryu AJ, Scott CG, Mandale DR, Naqvi TZ, Pellikka PA. Cardiac abnormalities in COVID-19 and relationship to outcome. Mayo Clin Proc 2021;96:932-42.
7. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. Nat Med 2021;27: 601-15.
8. Vehar S, Boushra M, Ntiamoah P, Biehl M. Post-acute sequelae of SARS-CoV-2 infection: caring for the “long haulers”. Cleve Clin J Med 2021;88: 267-72.
9. Baruch G, Rothschild E, Sadon S, Szekely Y, Lichter Y, Kaplan A, et al. Evolution of right and left ventricle functional and speckle-tracking echocardiography in patients recovering from coronavirus disease 2019: a longitudinal study. Eur Heart J Cardiovasc Imaging 2021. https://doi.org/10.1093/ehjci/jeab190.
10. Karagodin I, Singulane CC, Descamps T, Woodward GM, Xie M, Tucay ES, et al. Ventricular changes in patients with acute COVID-19

October 2022

Journal of the American Society of Echocardiography
infection: follow-up of the World Alliance Societies of Echocardiography (WASE-COVID) Study. J Am Soc Echocardiogr 2022;35:295-304.

11. Bieber S, Kraechan A, Hellmuth JC, Muenchhoff M, Scherer C, Schroeder I, et al. Left and right ventricular dysfunction in patients with COVID-19 associated myocardial injury. Infection 2021;49:491-500.

12. Lassen MCH, Skaarup KG, Lind JN, Alhakak AS, Sengelov M, Nielsen AB, et al. Recovery of cardiac function following COVID-19—ECHOVID-19: a prospective longitudinal cohort study. Eur J Heart Fail 2021;23:1903-12.

13. Mahajan S, Kunal S, Shah B, Garg S, Palleda GM, Bansal A, et al. Left ventricular myocardial strain in COVID-19 recovered patients. Echocardiography 2021;38:1722-30.

14. Ozer S, Candan L, Ozyildiz AG, Turan OE. Evaluation of left ventricular global functions with speckle tracking echocardiography in patients recovered from COVID-19. Int J Cardiovasc Imaging 2021;37:2227-33.

15. van den Heuvel FMA, Vos JL, van Bakel B, Duijnhouwer AL, van Dijk APJ, Dimitriu-Leen AC, et al. Comparison between myocardial function assessed by echocardiography during hospitalization for COVID-19 and at 4 months follow-up. Int J Cardiovasc Imaging 2021;37:3459-67.

16. Kaminski A, Payne A, Roemer S, Ignatowski D, Khandheria BK. Answering to the call of critically ill patients: limiting sonographer exposure to COVID-19 with focused protocols. J Am Soc Echocardiogr 2020;33:902-3.

17. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE statement on protection of patients and echocardiography service providers during the 2019 novel coronavirus outbreak: endorsed by the American College of Cardiology. J Am Soc Echocardiogr 2020;33:648-53.

18. Anand V, Thaden J, Pellikka PA, Kane GC. Safe operation of an echocardiography practice during the COVID-19 pandemic: single-center experience. Mayo Clin Proc 2021;96:531-6.

19. Celutkiene J, Pudil R, Lopez-Fernandez T, Grapsa J, Nihoyannopoulos P, Bergler-Klein J, et al. Role of cardiovascular imaging in cancer patients receiving cardiotoxic therapies: a position statement on behalf of the Heart Failure Association (HFA), the European Association of Cardiovascular Imaging (EACVI) and the Cardio-Oncology Council of the European Society of Cardiology (ESC). Eur J Heart Fail 2020;22:1504-24.

20. 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 2020;28:139.e14.

21. Voigt JU, Pedrizetti G, Lysiansky P, Marwick TH, Houle H, Baumann R, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. J Am Soc Echocardiogr 2015;28:183-93.

22. Thavendiranathan P, Poulin F, Lim KD, Plana JC, Woo A, Marwick TH. Use of myocardial strain imaging by echocardiography for the early detection of cardiotoxicity in patients during and after cancer chemotherapy: a systematic review. J Am Coll Cardiol 2014;63:2751-68.

23. Plana JC, Galdetesi M, Barac A, Ewer MS, Ky B, Scherrer-Crosbie M, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2014;27:911-39.

24. Karagodin I, Carvalho Singulane C, Woodward GM, Xie M, Tucay ES, Tude Rodrigues AC, et al. Echocardiographic correlates of in-hospital death in patients with acute COVID-19 infection: the World Alliance Societies of Echocardiography (WASE-COVID) Study. J Am Soc Echocardiogr 2021;34:819-30.

25. Rothschild E, Baruch G, Szekely Y, Lichter Y, Kaplan A, Taibb P, et al. The predictive role of left and right ventricular speckle-tracking echocardiography in COVID-19. JACC Cardiovasc Imaging 2020;13:2471-4.

26. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis 2020;94:91-5.

27. Raman B, Bluemke DA, Luscher TF, Neubauer S. Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus. Eur Heart J 2022;43:1157-72.

28. Carfi A, Bernabei R, Landi F. For the Gemelli against COVID-19 Post-Acute Care Study group. Persistent symptoms in patients after acute COVID-19. JAMA 2020;324:603-5.

29. Writing C, Gluckman TJ, Bhave NM, Allen LA, Chung EH, Spatz ES, et al. 2022 ACC expert consensus decision pathway on cardiovascular sequelae of COVID-19 in adults: myocarditis and other myocardial involvement, post-acute sequelae of SARS-CoV-2 infection, and return to play: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2022;79:1717-56.