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Evaluation of depression, anxiety, and stress symptoms and their relationship with subclinical myocardial dysfunction by left ventricular global longitudinal

Short Title: Psychological symptoms and myocardial damage in COVID-19

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) has had a great impact on patients' physical problems as well as psychological status. However, there is limited data about the impact of psychological problems on cardiac function during the COVID-19 pandemic. In this study, we aimed to investigate the relationship between mental health disorders and subclinical early myocardial systolic dysfunction by left ventricular global longitudinal strain (LVGLS) imaging in patients recovered from COVID-19.

Methods: Of the 108 participants**,** 71 patients had recovered from COVID-19; the members of the study group were prospectively recruited to the study after COVID-19 recovery. Comparisons were made with a risk-factor matched control group (n=37). The psychological status of the subjects, namely, Depression, Anxiety and Stress Scale-21 (DASS-21), and the Impact of Events Scale (IES-R) at follow-up visits, were assessed via questionnaire forms. The relationship between the psychological parameters and LVGLS values was subsequently evaluated.

Results: Overall, 45.0% of patients with COVID-19 had some degree of anxiety after recovery. A significant negative correlation was found between LVGLS and DASS-21 total score, DASS-21 anxiety subscale score, IES-R total score, and IES-R intrusion subscale score (r= -0.251, p=0.02; r= -0.285, p=0.008; r= -0.291, p=0.007; and r= -0.367, p=0.001**,** respectively). Furthermore, the DASS-21 total score was identified as an independent predictor of LVGLS (β= -0.186, p=0.03).

Conclusions: Patients who suffered from the COVID-19 disease may have experienced psychological distress symptoms due to COVID-19, which may be associated with silent impairment in myocardial systolic functions measured by global longitudinal strain analysis.

Keywords: COVID-19; Left ventricular global longitudinal strain; Depression; Anxiety; Stress.

INTRODUCTION

In December 2019, a novel coronavirus, known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), first emerged in Wuhan, China and rapidly spread globally, causing an international outbreak of a new form of pneumonia called coronavirus disease 2019 (COVID-19).[1] COVID-19 has caused a significant burden on multi-organ systems, first of all lungs and also has had a significant impact on individuals' psychological health. Therefore, it is important to manage the follow-up of recovered patients for early identification of possible organ damage and long-term consequences.

The COVID-19 outbreak has caused increased psychological problems such as stress, anxiety, and depression, both in patients and in the general population.[2,3] Cheng et al showed that among 60 patients with COVID-19 in a Wuhan hospital, the incidences of anxiety and depression were 47.5% and 27.1%, respectively.[4] Post-traumatic stress disorder (PTSD), anxiety, depression, and other psychological disturbances might be expected in COVID-19 patients, especially after intensive care unit admission.[5] Infected as well as non-infected people are prone to the development of psychological distress.[6,7] Misleading information about the new coronavirus disease, the number of infected patients, quarantine periods, and the deaths occurring throughout the course of the disease are some of the main causes of psychological distress in the COVID-19 pandemic.[8]

Healthy behaviors and mental status are critical for cardiac health. Psychological disorders can play a major role in the occurrence of cardiovascular diseases, which may lead to myocardial dysfunction and poor cardiac outcomes.[9] Coronary artery disease (CAD), myocardial dysfunction, and heart failure (HF) can all develop and progress due to psychological stress, anxiety, and depression in patients without previous cardiovascular disease.[9]

Anxiety disorders such as PTSD and depression have been found to be associated with an increased risk of HF.[10, 11, 12] In a previous study, the diagnosis of PTSD was linked with a 47% increased risk of HF over the subsequent seven years.[13] Similarly, depression was prospectively found to be associated with an 18% increased risk of HF development.[12] This relationship may be explained by several mechanisms, such as activation of the sympathetic nervous system and autonomic dysfunction.

Myocardial dysfunction may present as subclinical impairment of the left ventricular (LV) systolic function in patients with COVID-19.[14] Left ventricular global longitudinal systolic strain (LVGLS) measured by speckle-tracking echocardiography (STE) is a sensitive and objective method that two-dimensional (2D)-STE has demonstrated ability to identify subtle, preclinical impairments in systolic function that are undetectable by conventional imaging techniques, including LV ejection fraction (LVEF).[15] LVGLS analysis is very useful in estimating global LV myocardial tissue damage, and it provides prognostic information in many cardiovascular diseases.[16] For example, Liu et al reported that in type 2 diabetes mellitus (DM) patients without known cardiovascular disease (CVD), impaired GLS was associated with cardiovascular events including acute coronary syndrome, HF, or even cardiovascular death and provided incremental prognostic information to HbA1c levels.[17] Again, in another study, LV systolic longitudinal dysfunction in DM patients with preserved LVEF of ≥ 55%, as identified by GLS, was reported as a marker of a preclinical form of diabetic cardiomyopathy.[18] Also, LV longitudinal systolic dysfunction determined by GLS was found to be precede irreversible myocardial dysfunction and related overt HF in patients receiving cancer chemotherapy.[19]

In the present study, we aimed to investigate specific psychological symptoms such as stress, anxiety, and depression in patients who have recovered from COVID-19 using the Depression, Anxiety, and Stress Scale-21 (DASS-21) and the Impact of Event Scale (IES-R), and to evaluate whether these psychological problems had an impact on subclinical myocardial systolic dysfunction through LVGLS during the COVID-19 outbreak.

To the best of our knowledge, there has been no published study investigating the association between subclinical impairment in myocardial function by strain imaging and psychological status of patients recovered from COVID-19 infection.

METHODS

Study population

In the study group, 71 consecutive patients who recovered from COVID-19 infection were prospectively recruited to the study from a COVID-19 outpatient clinic between November 2020 and May 2021, while the control group consisted of 37 patients matching the study group in age, sex, body mass index (BMI), hypertension, controlled diabetes mellitus, psychiatric disorder, and smoking status. The diagnosis of COVID-19 had been confirmed by real-time reverse-transcriptase-polymerase chain reaction (RT-PCR) on samples taken from the respiratory tract of the participants. Written informed consent was obtained from all the subjects according to the Declaration of Helsinki. This single center, prospective, observational study was approved by the local Ethics Committee of Istanbul University (Decision no: 2020/11/208856).

Patients with CAD and acute coronary syndromes within 3 months, patients with an LVEF of <50%, severe valvular heart disease, atrial fibrillation, ≥ stage 2 hypertension, uncontrolled DM (HBA1c ≥8), chronic kidney disease (GFR <30 mL/min/1.73m^2), chronic liver disease, chronic obstructive pulmonary disease, chronic inflammatory diseases, a history of myocarditis, malignancy, pregnancy, thyroid disorder, and all other clinical conditions that may impair LV strain analysis, severe psychiatric disorders in which the reality of assessment and judgement is impaired, intellectual disability, alcohol and drug abuse, or cognitive disorders, and poor echogenicity were excluded from the study.

Study design

The study group included 71 consecutive patients who had recovered from COVID-19 infection, and comparisons were made with the control group (n= 37) that had no history of COVID-19 infection. The study group was further classified into 2 groups according to whether their recovery was at home (n=48) or in the hospital (n=23).

The clinical and demographic characteristics, and the control laboratory parameters of the patients were recorded at follow-up visits. Treatments received for COVID-19 infection and the image reports from chest computed tomography (CT) during hospital admission were retrospectively obtained from the hospital medical records of the COVID-19 patients. The severe pneumonia was identified with any of the following conditions in patients: bilateral lung infiltration of >50%, and/or multiple mottling and sub-pleural ground-glass opacity based on CT scan, respiratory rate ≥30/minute with hypoxemia; oxygen saturation ≤93% on room air.[20] Mild to moderate pneumonia was identified as the patients in the absence of clinical signs of severe pneumonia. Patients with severe respiratory distress requiring endotracheal intubation, hemodynamic instability with hypotension (systolic blood pressure <90 mmHg) and tachycardia (> 110 beats/minute), and signs of peripheral hypoperfusion were admitted to the intensive care unit (ICU).

A detailed echocardiographic examination was performed on all the patients during their cardiac status check. The median time interval after COVID-19 recovery to the day of cardiac ultrasound was 118 days (range, 30-197 days).

Additionally, on the day of echocardiography, the psychological status of the subjects was assessed via inventories. The Turkish versions of DASS-21 and IES-R were used to measure depression, anxiety, and stress levels, and to evaluate acute stress symptoms of the subjects, respectively.

Definitions

Patients were considered to have recovered from COVID-19 when discharged from the hospital or at the end of the quarantine period at home and they showed no symptoms of infection in addition to a negative swab test by RT-PCR on a respiratory tract sample.

Two-dimensional transthoracic echocardiography

During follow-up visits, transthoracic echocardiography (TTE) was performed on all the subjects by two experienced cardiologists blinded to the groups and their clinical data. The participants were examined in the left lateral decubitus position with an iE33xMATRIX ultrasound system (*Philips Medical Systems, Andover, Massachusetts*) using an X5–1 (1–5 MHz) transducer. Echocardiographic images were obtained in the parasternal and apical views using the techniques recommended by the American Society of Echocardiography.[21] LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LVEF were calculated using the biplane Simpson's method.[22] Left atrial volume index (LAVI) was calculated. LV diastolic function was assessed using the ratio of the peak early diastolic filling velocity (E) to the late diastolic filling velocity (A): E/A ratio, and the ratio of transmitral E to the mean of LV medial septal and lateral early diastolic tissue velocities (mean e'): E/e' ratio. Right ventricular (RV) function was determined by measuring tricuspid annular plane systolic excursion (TAPSE) in the RV free wall. Pulmonary artery systolic pressure (sPAP) was measured by tricuspid regurgitation peak velocity.

Two-dimensional speckle-tracking echocardiography

LV longitudinal systolic strain analysis was performed by 2D-STE to track the regions of interest. The apical four-, three-, and two-chamber views were obtained for strain imaging. All data were stored digitally and subsequently analyzed offline using a dedicated software (QLAb-CMQ) program. LVGLS was calculated as the mean of the peak strain values of apical four-, three-, and two-chamber views at aortic valve closure time for systolic strain analysis of the LV. In a meta-analysis, the normal values of GLS were reported to be varied from −15.9% to −22.1% (mean, −19.7%; 95% CI, −20.4% to −18.9%).[23] For the echocardiography laboratory of our institution, mean values of LVGLS obtained by the ultrasound system with QLAb-CMQ software program were −21.6% ± 2.9 in healthy volunteers.

Intra-observer and inter-observer reproducibility

Intra-observer reproducibility was calculated from repeated measurements performed by the same operator after 3 months, and inter-observer reproducibility by a second independent operator (EAG). Reproducibility was assessed using the intraclass correlation coefficient (ICC). The following levels of agreement were used: excellent for ICC >0.74, good for ICC 0.6-0.74, fair for ICC 0.4-0.59, and poor for ICC <0.4.[24] Inter-observer ICC was 0.89 (95% CI 0.806-0.937), and intra-observer ICC of strain parameters was 0.93 (95% CI 0.888-0.954), in this study.

Psychological evaluation in the study population

All participants were asked to fill out the forms and inventories by self-administration while waiting in the isolated lounge of the echocardiography unit prior to their echocardiography.

INVENTORIES:

1. **Screening Questionnaire***:* Designed by the investigators, this form consists of questions including socio-demographical characteristics such as age, sex, education level, marital status, lifestyle features, and questions about COVID-19 experience and opinions.

2. DASS-21: This self-report inventory evaluates psychological symptoms in the past week. DASS-21 consists of 21 questions on a 0–3 point scale. Depression, anxiety, and stress were measured as separate subgroups, with a total of seven questions each. Higher scores indicate a higher level of psychological distress. The scores are grouped in five levels ranging from normal to mild, moderate, severe, and extremely severe, according to different cut-off values.[25] This widely used tool has been translated into Turkish and validated for the Turkish population.[26]

3. IES-R: This is also a widely used self-report scale for screening distressful psychological symptoms associated with a traumatic life event. In our investigation, we changed the word “event” to “COVID-19 disease” in order to make it easier for the participants to understand the questions. IES-R consists of 22 items scored from 0 to 4 and three subscales, i.e.intrusion, avoidance, and hyperarousal. IES-R is not a diagnostic tool for post-traumatic stress disorder; however, higher scores indicate higher negative psychological reactions to the event.[27] The Turkish validity and reliability of this score was made by Çorapçıoğlu et al. in 2006.[28]

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences 26.0 version for *Windows* (*SPSS Inc.,* Chicago, IL, USA). The Kolmogorov–Smirnov test was used to test the normality of the data. Continuous data were expressed either as mean ± standard deviation (SD), or median (min-max); the categorical data were expressed as percentages. A chi-square test was used to evaluate the differences in categorical variables between the groups. A Student’s t-test or the Mann–Whitney U test was used to compare unpaired variables. The Pearson’s or Spearman’s correlation coefficients were calculated to evaluate the relationships among the parameters according to the normality of the data. Analysis of variance (ANOVA) was used to compare all reported data for parametric variables, while the Kruskal-Wallis test was performed for comparison among non-parametric variables between the groups. Multiple linear regression analysis of the association between echocardiographic left ventricle strain measurements, total DASS-21, and DASS-21 anxiety score, including age, sex, educational level, and marital status as independent variables, were performed. Standardized partial regression coefficients (β) were used to compare the effect on the dependent variable, and 95% confidence intervals (CI) were determined. Significance was taken at a two-sided $p < 0.05$.

RESULTS

Clinical and sociodemographic characteristics and COVID-19 related questions

The baseline and clinical characteristics of the subjects are presented in Table 1. The mean age of the total sample was 40.4 ± 10 years (42% male, 58% female). There were no significant differences between the groups in terms of age, sex, current smoking status, hypertension, DM, BMI, or psychiatric disorder. Among the 71 patients, 23 (32%) who had pneumonia on CT images required hospitalization and 48 (68%) recovered at home (Fig 1). Nineteen of the 23 (82.6 %) hospitalized patients had severe pneumonia. In our study, 4 patients (3.7%) were admitted to the ICU during hospitalization and underwent orotracheal intubation (Table 1). The median length of stay in the ICU was 13 days (range, 2-23 days), and duration of intubation was 5 days (range, 2-16 days). In our study, the median time of hospital stay duration was 32 days (range, 2-44 days) and average disease duration at home was 10 days. The patients received treatment according to the treatment guideline of the Ministry of Health in the early period of the COVID-19 pandemic. Table 2A shows the socio-demographic characteristics of the study participants. The majority of participants (71%) were married. In terms of educational level, 41.7% had a university degree with a statistical significance. The majority of respondents (87.9%) lived with a partner or housemate, 6.5% were sole occupants, and 5.6% lived with their family or children. A total of 23.1% were smokers and 10.3% consumed alcohol. A total of 13% had psychiatric disorders without statistical significance between the groups. The majority of respondents (72.2%) in the study group worried about COVID-19 re-infection, and most of the respondents (60.2%) declared that they had enough knowledge about COVID-19.

IES-R and DASS-21 scores of participants

DASS-21 and IES-R scores were compared between the study and control groups via questionnaires (Table 2B). Significant differences emerged between the groups based on the total DASS-21 score (p=0.005) (Table 2B, Fig. 2). Furthermore, DASS-21 anxiety subscale score was significantly different between the groups (p<0.001) (Table 2B, Fig.2). No group differences were found with the DASS-21 depression and stress subscale scores.

When IES-R total score and subscales were evaluated, significant differences among the groups were found with the IES-R total score (p=0.024), IES-R intrusion subscale (p=0.01), and IES-R hyperarousal subscale (p=0.024) (Table 2B, Fig.2). The median IES-R total score was significantly higher in hospitalized patients than those treated at home and controls (p=0.024). A trend toward significance appeared for the IES-R avoidance subscale (p = 0.078) (see Table 2B).

Echocardiographic characteristics

Table 1 shows the comparison of the echocardiographic parameters of the home recovery, the hospital recovery, and the control groups. Left atrial (LA) diameter was higher in the hospital recovery group compared to the controls (p=0.045). E/A ratio was significantly lower in the hospital recovery group compared to the home recovery group and the controls (p<0.001). LVEDV, LVESV, LVEDD, LVEF, LAVI, E/e'ratio, TAPSE and sPAP were similar between the groups. The LVGLS values of the control, home recovery, and hospital recovery groups were -17.8 ±

2.7%, -15.5 ± 3.7%, and -15.1 ± 2.8%, respectively (p=0.002). LVGLS values were significantly lower in the study group than in the control group (Fig. 3).

In correlation analysis, LVGLS was significantly negatively correlated with DASS-21 total score, DASS-21 anxiety subscale score, IES-R total score, and IES-R intrusion subscale score (r = -0.251, p = 0.02; r = -0.285, p = 0.008; r = -0.291, p = 0.007; and r = -0.367, p = 0.001**,** respectively) (Table 3, Fig 4).

We also classified total patients into 2 subgroups as patients with comorbid disease including hypertension, DM, psychiatric disorders, or hospitalization and patients with severe pneumonia, and evaluated the correlations of LVGLS with psychological scores in each subgroups.

We found a significant higher negative correlation between LVGLS values and IES-R total, and IES-R intrusion score in comorbidity group (r = -0.495, p = 0.001; r = -0.470, p = 0.002; respectively) and in severe pneumonia group (r = -0.716, p = 0.002; r = -0.666, p = 0.004; respectively) (Table 4, Fig 5, 6). Moreover, a significant negative correlation was found between LVGLS values and IES-R hyperarousal score in comorbidity and severe pneumonia group (r = -0.419, p = 0.006; r = -0.500, p = 0.041; respectively) (Table 4).

There was no significant correlation between DASS-21, and IES-R scores, and subscales and the other conventional echocardiographic parameters (Table 5).

In terms of sociodemographic characteristics, there was a statistically significant correlation between LVGLS and age, sex, BMI, educational level, and marital status. ($r = -0.329$, $p = 0.005$; $r = -0.213$, $p = 0.044$; $r = -0.461$, $p < 0.001$; $r = 0.381$, $p < 0.001$; $r = -0.273$, $p = 0.01$ respectively) (Table 6). LVGLS values were found to be lower in the male sex in our study. Interestingly, there was a negative correlation between marriage and LVGLS.

In the multivariate linear regression analysis, educational level (β=1.432, 95% CI 0.350 to 2.514, p=0.01) and DASS-21 total score (β = -0.186, 95% CI -0.354 to -0.018, p=0.03) were found to be independent predictors of LVGLS (Table 7).

DISCUSSION

The efficient follow-up of COVID-19 survivors is of high importance,. Due to the COVID-19 disease, many patients have experienced both physical difficulties and psychological distress, requiring a multidisciplinary evaluation.[8] This study investigated the mental health disorders such as depression, anxiety, and stress in recovered COVID-19 patients and also evaluated the relationship between psychological parameters and early subclinical myocardial dysfunction by 2D-STE strain imaging method, for the first time. The present study demonstrated that psychological status of patients may be associated with silent impairment in myocardial functions measured by GLS analysis.

The COVID-19 pandemic may have caused mental health disorders such as depression, anxiety, and acute or chronic stress symptoms in patients. In a meta-analysis, the percentage of anxiety and depression symptoms in COVID-19 patients was found to be significantly higher than that of the public.[29] In our study, the psychological status of depression, anxiety, and stress was highlighted by DASS-21 scale, and acute stress symptoms by IES-R. According to our findings, the numbers of patients reporting anxiety symptoms were higher in the COVID-19 group than in the controls. In addition, DASS-21 total and anxiety subscale scores were found to be significantly higher in COVID-19 patients compared to controls. Our findings suggest that patients who suffered from COVID-19 may be more prone to develop anxiety after recovery. Because of the high total score of IES-R in the hospital recovery group, we considered that these patients have had more traumatic experiences and related psychological distress symptoms due to the COVID-

19 disease. Additionally, COVID-19 patients reported higher levels of intrusion and hyperarousal regarding acute stress symptoms.

Ferraris et al reported higher traumatic experiences associated with higher depression and anxiety scores in recovered COVID-19 patients.[30] Kong et al described that among 144 hospitalized patients with SARS-CoV-2 infection, 34.7% and 28.5% of subjects had high anxiety and depression scores, respectively.[31] Also, Giurgi-Oncu et al found higher anxiety and depression symptoms in hospitalized patients than outpatients.[32]

Huang et al reported that all hospitalized patients, especially those developing severe clinical COVID-19 disease, experienced more distress, anxiety, and depression problems.[33] Contrary to their results, Ferraris et al found no significant association between severity of COVID-19 disease and psychological symptoms in patients.[30] However, they reported higher anxiety or depression symptoms in post-COVID-19 patients than normative population.[30]

As observed by previous studies, of the 71 recovered COVID-19 patients, 45.0% reported anxiety symptoms, 21.1% reported depression, and 12.7% had stress symptoms in our study. The hospital recovery group had a higher number of patients with severe depression and mild levels of anxiety. In our study, recovered COVID-19 patients exhibited higher scores in anxiety and acute stress reactions, such as intrusion and hyperarousal, revealing that the patients were psychologically affected by COVID-19. The disease may have been perceived by the patients as traumatic events, resulting in various psychiatric morbidities.[34]

The physical consequences of the deadly disease itself, social isolation, quarantine conditions, financial difficulties, re-infection risks, worrying about family members being infected, and not having a proper consensus on both treatment and prevention strategies could result in an increase in the anxiety levels of individuals.[35] In addition, people who have passed through the disease and have had a challenging treatment history either in the hospital or at home may have additional psychological stress reactions. In our sample, two groups of acute stress symptoms—intrusion and hyperarousal—were found to be elevated. Intrusion is the state of re-experiencing a traumatic event through symptoms like distressing dreams or flashbacks. Hyperarousal includes mostly physical subjective conditions such as difficulty falling asleep, irritability, increase in heart and respiration rates, and exaggerated startle responses.

The symptoms are expected to decrease over time; however, if they persist, they may evolve to PTSD.[36] In a previous pandemic, SARS survivors had depression, stress, anxiety, or PTSD not only in acute phase but also one year after the outbreak.[37] Wu et al reported a prevalence of PTSD of 5% at 3-month follow-up after hospital discharge in SARS survivors[38], whereas it was found to be high as 25.6% at a 30-month follow-up study.[39] In another recent study, chronic illnesses, length of hospitalization, ICU treatment were found to be associated with the development of PTSD among COVID-19 survivors, after discharge.[40] Again, in a study of Wesemann et al, PTSD symptoms have been reported to be high especially in hospitalized high-risk COVID-19 patients.[41] Therefore, it is important to identify the patients who exhibit initial psychological disturbances in order to refer them for further mental evaluation and support.

The DASS-21 depression and stress scores did not show a significant difference within the groups. Several explanations may be given for this finding. First, this scale evaluates the symptoms experienced by an individual within the past week. Participants may have experienced depressive symptoms during their treatment period or afterwards; however, the symptoms may have decreased during the follow-up period. Second, individuals' supportive personality characteristics, functional coping abilities, and psychological resilience may have a preventive role in combating depression.[42]

The discrepancy between DASS-21 stress subscale scores and IES-R scores is noteworthy; while the IES-R focuses only on the particular COVID-19 event, the DASS-21 stress subscale includes questions in a general manner. We may have noticed the distressful experiences that are related to COVID-19.

There are various clinical studies investigating the association of psychological status with CVD. Previous studies showed that psychological problems such as anxiety disorders and depression have been found to be associated with CAD, myocardial dysfunction, and HF.[9] In a prospective study, the diagnosis of PTSD was associated with a 47% increased risk of HF over the subsequent seven years.[13] Again, another study showed a significant relationship between coronary ischemia and psychological symptoms.[43]

Some of the possible pathophysiological mechanisms between psychological distress and cardiovascular diseases are a high sympathetic tone, an increase in cortisol and catecholamine levels, an increased release of inflammatory markers, endothelial dysfunction, abnormal platelet activation, and an accelerated atherogenesis.[44]

According to previous studies, psychological distress symptoms with longer durations were found to be associated with an increase in both proinflammatory cytokines such as interleukin (IL)-6, tumor necrosis factor-alpha (TNF-α) and sympathetic system activity occurring as a stress response that may negatively affect myocardial systolic function.[45] Some studies have found a relationship between anxiety and higher levels of C-reactive protein (CRP), IL-6, and TNF-α.[46]
One of the possible mechanisms of myocardial dysfunction and HF is autonomic dysfunction. Psychological symptoms have been associated with an imbalance in autonomic nervous system function, such as sympathetic hyperactivity and parasympathetic hypoactivity.[47] This autonomic imbalance may lead to cardiac remodeling and myocardial dysfunction as seen in Takotsubo syndrome (TS), which is an acute stress-induced cardiomyopathy. In an experimental study, immobilization stress of rats has exhibited electrocardiographic and left ventriculographic changes seen in TS, preventing by combined blockade of α- and β-adrenoceptors.[48]

There is no sufficient data about the effect of psychological stress on subclinical cardiac dysfunction. One *HUNT* trial showed that depression symptoms, especially in women, can affect subclinical systolic function measured by GLS.[49] However, its relationship with anxiety has not sufficiently been clarified.

According to our findings, we found a negative correlation between LVGLS values and DASS-21 total score, DASS-21 anxiety subscale score, IES-R total, and IES-R intrusion subscale scores in total patients. The relationship was statistically significant, but we could not show high statistical correlation. Due to the small sample size of the study cohort, clinical significance appears limited. However, similar to our findings, in a previous study, Frasure-Smith et al found a lower significant correlation value between CRP levels and depression scores in coronary heart disease patients ($r = 0.11$, $p = 0.004$).[50] Again, a meta-analysis showed similar correlation effects to our results between psychological symptoms and flow-mediated dilatation which is an indicator of endothelial function ($r = -0.22$, $p = 0.06$).[51] Moreover, Sawatari et al found similar negative correlation value to our results between LVEF levels and IES-R scores in patients with implantable cardioverter-defibrillators ($r = -0.36$, $p = 0.045$).[52]

Although we observed lower correlations in total patient population, we found higher significantly correlation coefficients between LVGLS values and IES-R total, and intrusion scores in patients admitted with severe pneumonia and also having comorbidity. Therefore, we may speculate that patients with comorbid diseases, or recovering from the severe illness with challenging treatment history of COVID-19 may have experienced more psychological stress reactions which may have had a more negative impact on subclinical myocardial systolic functions. Our study results may be consistent with Tarsitani et al showing an association of severity of COVID-19 with PTSD in discharged patients.[40] Likewise, in a recent study of Giurgi-Oncu et al found hospitalized patient group to have worse echocardiographic parameters together with psychological distress symptoms in post-acute COVID-19 patients.[32]

Since the psychological distress symptoms could change with different duration of the disease, we will need longer follow-up data, which is one of the main limitations of this study.

The present study also showed that an increase in the total DASS-21 score was an independent predictor of decreased LVGLS, in multivariate regression analysis. However, we found no significant associations between conventional echocardiographic parameters and psychological scores.

In our study, LVGLS was significantly positively correlated with educational level, being an independent predictor of LVGLS. Some studies indicating the inverse relationship between educational level and psychological distress may support our findings.[53] Educational level represents individuals' abilities in accessing information about the disease, those with the capability of interpretation of symptoms, and dealing with the stress. In addition, this study showed an inverse relationship between LVGLS levels and marital status. There was a negative correlation between marriage and LVGLS. The deterioration of the home arrangement due to quarantine conditions and disease-related concerns about family members may have caused negative psychological effects in married individuals. An accurate interpretation of the relationship between socio-demographic characteristics and LVGLS values requires further evaluation for real clinical significance. The social factors for myocardial functions in this regard seem to be important. However, we found higher correlation between the BMI and LVGLS values than the other socio-demographic parameters. We know that obesity and a high BMI are associated with an increased risk of developing LV systolic and diastolic dysfunction.[54]

As a result, we suggest that psychological distress symptoms regarding traumatic experiences due to the COVID-19 disease in recovered patients may have had a negative impact on myocardial functions and may be related to myocardial damage. An other possible explanation could be that worse psychological distress symptoms are present in more severe COVID-19 disease. Then the impact on myocardial function could be directly related to and even induced by the severity of viral infection. In this case the psychological symptoms could be considered as a surrogate indicator, more than a cause/effect relationship, paralleling such severity.

It is difficult to make definite conclusions regarding the small sample size of the study population and having no longer follow-up data, however, we may speculate that the screening of the psychological symptoms can be important for achieving better control of the possible psychiatric disorders and future cardiac outcomes. Also, young age, female sex, having no severe COVID-19 disease, or chronic illnesses, and higher educational level may be the favorable factors for the possible related cardiac outcomes. The use of psychological counseling methods and the offer of psychological support would be effective ways to improve patients' clinical conditions.

Although the number of patients of our study is limited, it may be suggested that our study made an important contribution to clinical practice about COVID-19 with emphisis on the importance of subclinical LV systolic strain analysis in the cardiac risk prediction of the patients with psychological distress. Our results need future investigations.

Strengths of the Study

Our study has some strengths. To date, there have been no available studies investigating the influence of mental health disorders of the recovered COVID-19 patients on the early subclinical myocardial systolic dysfunction. We consider our study findings to be important in this sense. We could obtain echocardiographic data and questionnaires for psychological evaluation on the same date. Besides, we compared our results with non-COVID controls. Also, participants were not excluded from the study if they had any psychiatric disorder since the analyses were focused on the relationship between levels of mental health disorders due to COVID-19 and cardiac outcomes. So, we may have increased the strength of our study findings.

Limitations of the Study

This study has some limitations. First, it has a small sample size regarding clinical significance of study results since it is a single center study. Second, the forms were self-administrative, thus the psychological parameters were obtained from individuals' subjective responses instead of a structured psychiatric examination conducted by a trained psychiatrist. People may have evaluated their mental states in a better or worse state than actual, due to either a lack of insight and an unconscious defense mechanism or by purpose. Third, we don't have clinical endpoints such as mortality or cardiac morbidity. Finally, this is a cross-sectional study and patients were recruited over a short period. We have no long-term follow-up data for assessing the progression of psychological symptoms.

Conclusions

In conclusion, the COVID-19 disease can deteriorate mental health status of people. An effective psychological intervention at the early stages may ensure improvement in psychological symptoms. Also, the assessment of mental health status and psychological distress symptoms could be important for reducing possible future cardiac events and taking preventive strategies. Thus, our findings may well have clinical implications for better management of recovered COVID-19 patients who suffered from psychological distress. We suggest that those patients may require a multidisciplinary approach in their further treatment, including cardiac care. Our study findings should be confirmed with follow-up data of a larger population by future studies.

Author Contributions: D.B., and I.P.; conceived the idea for the article, framing the hypothesis, D.B., Z.B., and E.A.G.; designed the methods to generate results, T.T., B.U., and Z.B.; supervision of the project and the manuscript, P.K.O., E.B.K, and D.B.; resources acquisition, S.B.K., Y.C., and P.K.O.; materials and referring patients, I.P., A.M., and Y.C.; data collection and processing data, E.A.G., I.P., and P.K.O.; data analysis and interpretation, A.M., S.B.K., and E.B.K.; literature search, E.A.G., I.P., and D.B.; writing-original draft preparation, T.T., B.U., and Z.B.; critical review and editing, A.M., Y.C., and E.B.K.; other contributions to this work. All authors have read and approved the paper.

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Declaration of Conflicting Interests:

The authors declared that there was no potential conflicts of interest for this manuscript.

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FIGURE LEGENDS

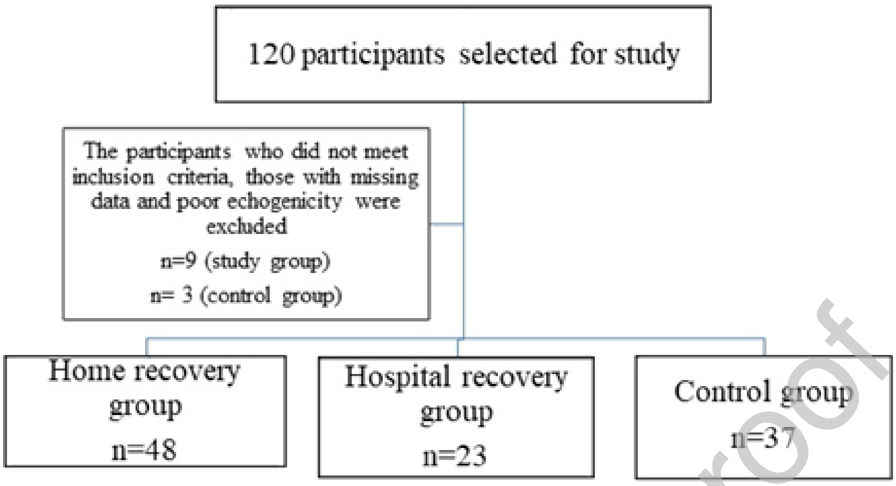


Figure 1. Flow chart of the study population.

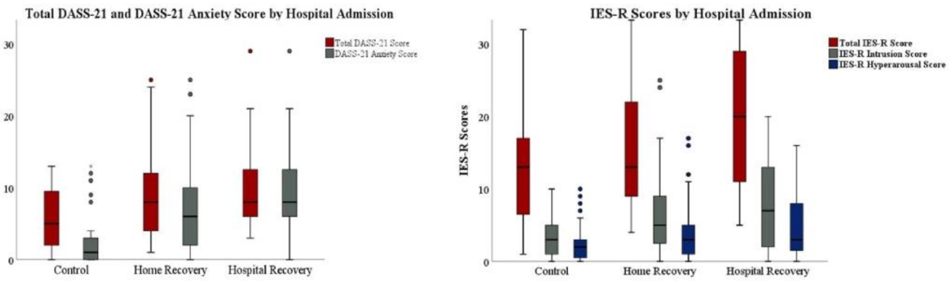


Figure 2A

Figure 2B

Abbreviations: DASS-21 Depression, Anxiety and Stress Scale, IES-R Impact of Event Scale-Revised

Figure 2 (a) Total DASS-21 and DASS-21 Anxiety scores according to hospital admission of the study group. (b) Total IES-R, IES-R intrusion and hyperarousal scores according to hospital admission of the study group.

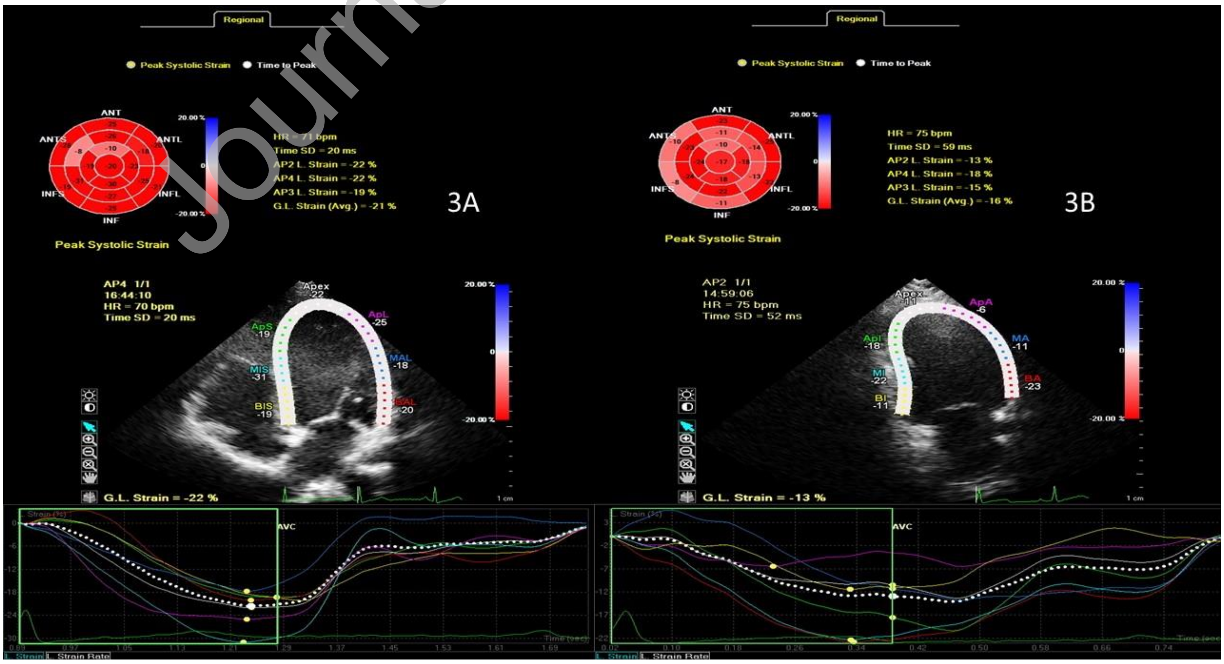
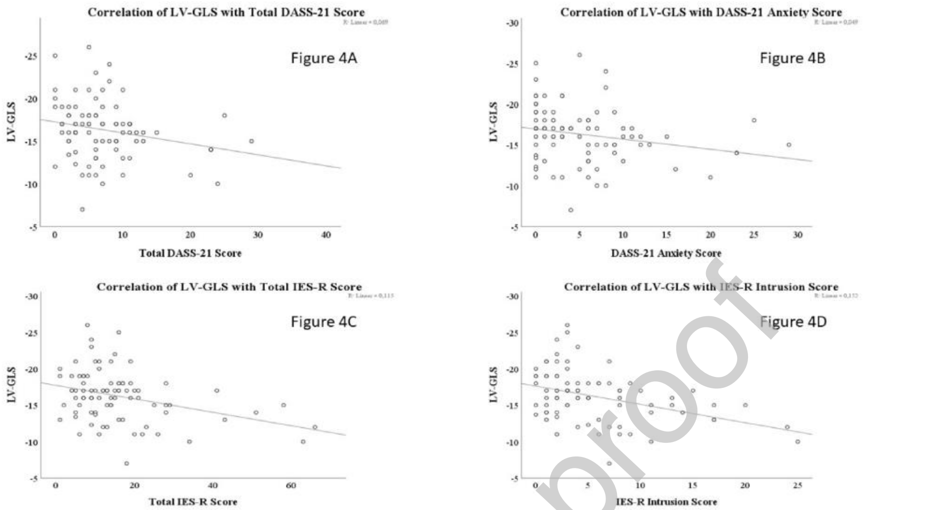


Figure 3. Bull's eye images of left ventricular global longitudinal strain (LVGLS) of control (a) and study groups (b).



Abbreviations: LV-GLS left ventricular global longitudinal strain, DASS-21 Depression, Anxiety and Stress Scale, IES-R Impact of Event Scale-Revised

Figure 4 (a) Correlation of LVGLS with Total DASS-21 Score. (b) Correlation of LVGLS with DASS-21 Anxiety Score. (c) Correlation of LVGLS with Total IES-R Score. (d) Correlation of LVGLS with IES-R Intrusion Score.

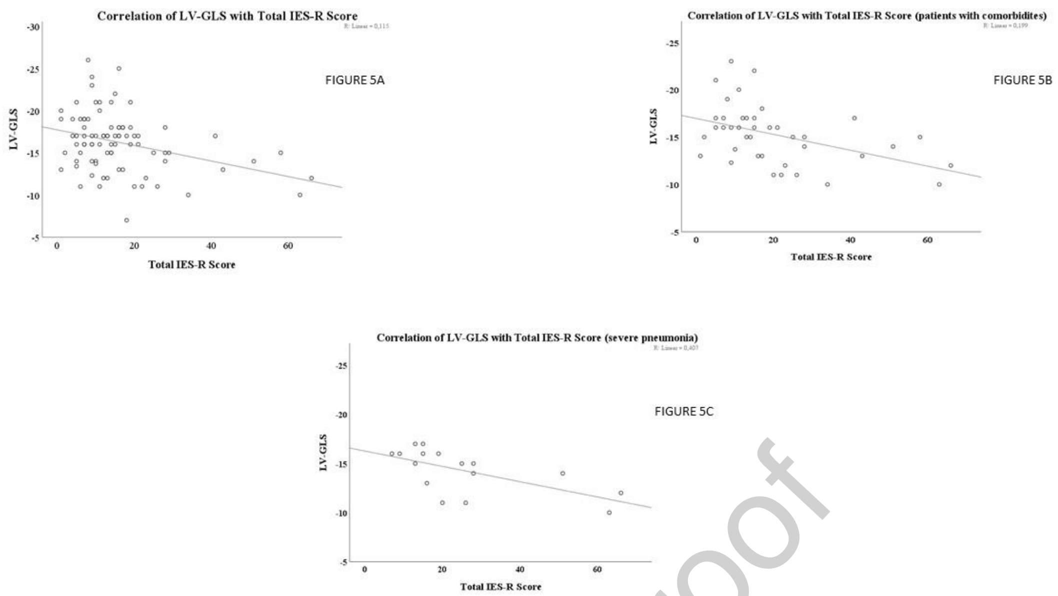


Figure 5 Abbreviations: LV-GLS left ventricular global longitudinal strain, IES-R Impact of Event Scale-Revised

Figure 5 (a) Correlation of LVGLS with Total IES-R Score. (b) Correlation of LVGLS with Total IES-R Score in patients with comorbidities. (c) Correlation of LVGLS with Total IES-R Score in patients with severe pneumonia.

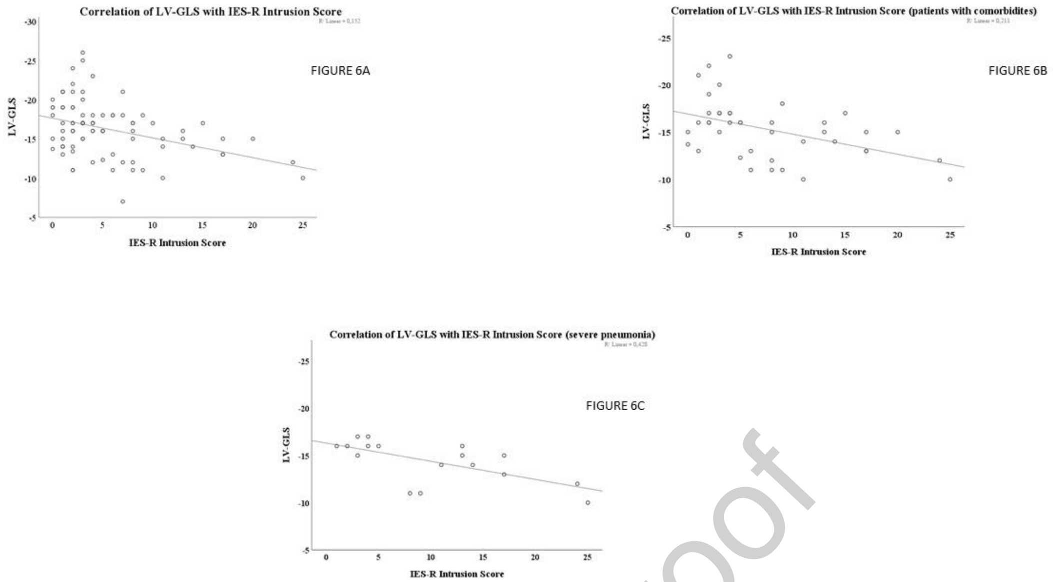


Figure 6 Abbreviations: LV-GLS left ventricular global longitudinal strain, IES-R Impact of Event Scale-Revised

Figure 6 (a) Correlation of LVGLS with IES-R Intrusion Score. (b) Correlation of LVGLS with IES-R Intrusion Score in patients with comorbidities. (c) Correlation of LVGLS with IES-R Intrusion Score in patients with severe pneumonia.

Table 1. Baseline clinical characteristics, treatment regimen, laboratory and echocardiographic findings of home-recovery, hospital-recovery and control groups.

	Total patients (n=108)	Control (n=37)	Home recovery (n=48)	Hospital recovery (n=23)	p- value
Clinical characteristics					
Age, (years)	40.4 ± 10	38.2 ± 7.7	42.4 ± 11.8	40.6 ± 9	0.181
Sex					0.192
Male n, (%)	45 (41.7 %)	11 (29.7 %)	23 (47.9 %)	11 (47.8 %)	
Female n, (%)	63 (58.3 %)	26 (70.3 %)	25 (52.1 %)	12 (52.2 %)	
HT, n(%)	24 (22.2 %)	5 (13.5 %)	10 (20.8 %)	9 (39.1 %)	0.065
DM, n(%)	13 (12 %)	4 (10.8 %)	3 (6.3 %)	6 (26.1 %)	0.053
BMI (kg/m^2)	28.5 ± 4.5	28.7 ± 3.9	27.9 ± 4.9	29.2 ± 4.1	0.052
Psychiatric disorder, n(%)	14 (13 %)	4 (10.8 %)	6 (12.5 %)	4 (17.4 %)	0.755
Smoking, n(%)	25 (23.1 %)	13 (35.1 %)	9 (18.8 %)	3 (13 %)	0.089
Pneumonia on CT	63 (58.3 %)	-	40 (83.3 %)[c]	23 (100 %)[c]	0.004*
Follow-up durations, (days)	118 (30-197)	-	110 (37-191)[c]	155 (31-197)[c]	0.005*
Hospital stay, (days)	32 (2-44)	-	0[c]	32 (2-44)[c]	<0.001*
Laboratory findings on the day of follow-up visits					
Fasting Plasma Glucose (mg/dl)	100 ± 28.1	94.9 ± 27.2[b]	97.6 ± 22.1[c]	111.9 ± 36.6[b,c]	0.027*
BUN (mg/dl)	13.3 ± 5.4	11.8 ± 4.5[b]	13.3 ± 5.5	15.2 ± 5.9[b]	0.036*

Creatinine (mg/dl)	0.7 ± 0.2	0.7 ± 0.2	0.8 ± 0.2	0.9 ± 0.3	0.137
AST (U/I)	18.1 (10-83)	17.7 (11-83)	18.1 (12-69)	18.5 (10-68)	0.798
ALT (U/I)	17.7 (5-97)	16.1 (7-62)	16.1 (6-87)	21.5 (5-97)	0.462
LDH (U/I)	189.9 ± 41.1	170.1 ± 33.7[a,b]	190 ± 29.1[a]	216.7 ± 55.0[b]	0.001*
Hgb (gr/dl)	13.3 ± 1.7	13.6 ± 1.3	13.1 ± 1.6	13.1 ± 2.2	0.331
WBC (10^3/µl)	6.6 (2.4-19.6)	6.8 (3.9-12.4)	6 (3.4-10.8)	7 (2.4-19.6)	0.177
Lymphocytes (10^3/µl)	2.2 (0.5-6.3)	2.2 (1.1-6.3)	2.2 (1-3.8)	2.1 (0.5-4.1)	0.397
CRP (mg/L)	1.8 (0-39)	1.4 (0-28)[b]	1.5 (0-17)[c]	6.1 (1-39)[b,c]	0.003*
D-dimer (µg/L)	320 (169-4810)	280 (169-560)	275 (190-1230)	390 (180-4810)	0.051
Ferritin (ng/ml)	54 (4-1010)	42.5 (6-246)[b]	40.7 (4-358)[c]	83.9 (11-1010)[b,c]	0.027*
Hs-troponin-T (pg/ml)	3.8 (3-59)	3 (3-5)[b]	3.5 (3-59)[c]	7.7 (3-41)[b,c]	<0.001*
Pro-BNP (pg/ml)	63.3 (5-1674)	33.1 (5-97)	66.3 (5-1674)	72.9 (5-1258)	0.114
Treatment					
Hydroxychloroquine, (%)	48 (44.4 %)	-	26 (54.2 %)[c]	22 (95.7 %)[c]	<0.001*
Azithromycin, n(%)	20 (18.7 %)	-	3 (6.3 %)[c]	17 (77.3 %)[c]	<0.001*
Favipiravir, n(%)	30 (28 %)	-	16 (33.3 %)[c]	14 (63.6 %)[c]	0.040*
Heparin, n(%)	27 (25 %)	-	6 (12.5 %)[c]	21 (91.3 %)[c]	<0.001*
Steroid, n(%)	6 (5.6 %)	-	1 (2.1 %)[c]	5 (21.7 %)[c]	0.019*
Immune modulator, n(%)	14 (13 %)	-	1 (2.1 %)[c]	13 (56.3 %)[c]	<0.001*

Antibiotics, n(%)	25 (23.1 %)	-	9 (18.8 %)[c]	16 (69.6 %)[c]	<0.001*
ICU admission, n(%)	4 (3.7 %)	-	0 (0%)[c]	4 (17.4 %)[c]	0.009*
NIMV/HFNC ,n(%)	8 (7.4 %)	-	0 (0 %)[c]	8 (34.8 %)[c]	<0.001*
Orotracheal intubation	4 (3.7%)	-	0 (0%)[c]	4 (17.4 %)[c]	0.009*
Echocardiographic Findings					
LVEDV (ml)	136.6 ± 23.3	131.9 ± 19.7	137.6 ± 23.7	142.1 ± 26.9	0.264
LVESV (ml)	54.6 ± 13.1	51.4 ± 11.3	56.9 ± 14.5	55.1 ± 12.2	0.203
LVEDD (mm)	45.2 ± 3.7	44.5 ± 3.2	45.3 ± 3.8	46 ± 4.3	0.264
LVEF (%)	64.8 ± 4.9	65.8 ± 4.9	63.9 ± 5.1	64.8 ± 4	0.364
LAVI (ml/m²)	20.9 ± 7	21.1 ± 5.8	21.4 ± 8.5	19.4 ± 5.6	0.690
LA (mm)	35.2 ± 4.5	33.8 ± 3.5[b]	35.3 ± 4.7	37.2 ± 4.6[b]	0.045*
E/A ratio	1.1 ± 0.3	1.3 ± 0.3[a,b]	1 ± 0.3[a,c]	0.8 ± 0.3[b,c]	<0.001*
E/e' ratio	8.2 ± 2.9	7.4 ± 1.9	8.3 ± 3.3	9.2 ± 3.2	0.061
TAPSE (mm)	21 ± 3.4	21.1 ± 3.2	20.9 ± 3.7	20.9 ± 3.3	0.940
SPAP (mmHg)	25.7 ± 5.2	24.9 ± 4.5	25.8 ± 5.8	26.4 ± 4.9	0.645
LVGLS (%)	-16.2 ± 3.4	-17.8 ± 2.7[a,b]	-15.5 ± 3.7[a]	-15,1 ± 2.8[b]	0.002*

Abbreviations: HT: hypertension, DM: diabetes mellitus, BMI body mass index, BUN: blood urea nitrogen, AST: aspartate transaminase, ALT: alanine transaminase, LDH: lactate dehydrogenase,Hgb: hemoglobin, WBC: white blood cell, CRP: C reactive protein, Hs-troponin-T: high sensitive-troponin-T, Pro-BNP: prohormone B-type natriuretic peptide, ICU: intensive care unit, NIMV: non invasive mechanical ventilation, HFNC: high flow nasal cannula, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end sistolic volume, LVEDD: left ventricular end diastolic diameter, LVEF: left ventricular ejection fraction, LAVI: left atrium volume index, LA: left atrium, TAPSE: tricuspid annular plane systolic excursion, sPAP: systolic pulmonary artery pressure, LVGLS: left ventricular global longitudinal strain

*If there is $p<0.05$ as the significance level, P^a:,control vs home recovery, P^b: control vs hospital recovery, P^c: home recovery vs hospital recovery

Table 2A. Comparison of socio-demographic and clinical characteristics between the groups.

	Total Patients (n=108)	**Control (n=37)**	**Home Recovery (n=48)**	**Hospital Recovery (n=23)**	**p-value**
Age (years)	40.4 ± 10	38.2 ± 7.7	42.4 ± 11.8	40.6 ± 9	0.181
Sex					
Male (n, %)	45 (41.7 %)	11 (29.7 %)	23 (47.9 %)	11 (47.8 %)	0.192
Female (n, %)	63 (58.3 %)	26 (70.3 %)	25 (52.1 %)	12 (52.2 %)	
Educational Level					
Primary School (n, %)	38 (35.2 %)	3 (8.1 %)[a,b]	25 (52.1 %)[a]	10 (43.5 %)[b]	<0.001*
High School (n, %)	25 (23.1 %)	6 (16.2 %)	11 (22.9 %)	8 (34.8 %)	0.253
University (n, %)	45 (41.7 %)	28 (75.7 %)[a,b]	12 (25 %)[a]	5 (21.7 %)[b]	<0.001*
Marital Status					
Single (n, %)	24 (22.4 %)	13 (35.1 %)[b]	9 (19.1 %)	2 (8.7 %)[b]	0.042*
Married (n, %)	76 (71 %)	22 (59.5 %)	36 (76.6 %)	18 (78.3 %)	0.193
Divorced or Widowed (n, %)	7 (6.5 %)	2 (5.4 %)	2 (4.3 %)	3 (13 %)	0.345
Home Arrangement					
Sole Occupant (n, %)	7 (6.5 %)	5 (13.5 %)	2 (4.3 %)	0 (0 %)	0.081
With Partner/ Housemate (n,%)	94 (87.9 %)	29 (78.4 %)	42 (89.4 %)	23 (100 %)	0.053
With Family/ Children (n, %)	6 (5.6 %)	3 (8.1 %)	3 (6.4 %)	0 (0 %)	0.395

Smoking (n, %)	25 (23.1 %)	13 (35.1 %)	9 (18.8 %)	3 (13 %)	0.089
Alcohol Use (n, %)	11 (10.3 %)	7 (19.4 %)[b]	4 (8.3 %)	0 (0 %)[b]	0.047
Comorbidity (n, %)	47 (43.5 %)	10 (27 %)[b]	20 (41.7 %)[c]	17 (73.9 %)[b,c]	0.002*
Psychiatric disorder, (n, %)	14 (13 %)	4 (10.8 %)	6 (12.5 %)	4 (17.4 %)	0.755
Informed about COVID-19	65 (60.2 %)	30 (81.1 %)[a,b]	25 (52.1 %)[a]	10 (43.5 %)[b]	0.005*
Anxiety about re-infection	52 (72.2 %)	-	39 (83 %)	18 (78.3 %)	0.634

*If there is p<0.05 as the significance level, P[a]:,control vs home recovery, P[b]: control vs hospital recovery P[c]: home recovery vs hospital recovery

Table 2B. Comparison of scales of depression, anxiety and stress and impact of event between the groups.

	Total Patients (n=108)	**Control (n=37)**	**Home Recovery (n=48)**	**Hospital Recovery (n=23)**	**p-value**
Total DASS-21 Score	7 (0-44)	5 (0-13)[a,b]	8 (1-44)[a]	8 (3-38)[b]	0.005*
DASS-21, Depression Score	1 (0-15)	1.5 (0-7)	1 (0-15)	2 (0-13)	0.623
DASS-21 Depression					
Normal (n, %)	87 (80.6 %)	31 (83.8 %)	38 (79.2 %)	18 (78.3 %)	0.826
Mild (n, %)	6 (5.6 %)	4 (10.8 %)	1 (2.1 %)	1 (4.3 %)	0.211
Moderate (n, %)	9 (8.3 %)	1 (2.7 %)	6 (12.5 %)	2 (8.7 %)	0.268
Severe (n, %)	2 (1.9 %)	0 (0 %)[b]	0 (0 %)[c]	2 (8.7 %)[b,c]	0.023*
Extremely Severe (n, %)	4 (3.7 %)	1 (2.7 %)	3 (6.3 %)	0 (0 %)	0.394
DASS-21 Anxiety Score	5 (0-38)	1 (0-13)[a,b]	6 (0-25)[a]	8 (0-38)[b]	<0.001*

DASS-21 Anxiety					
Normal (n, %)	71 (65.7 %)	32 (86.5 %)[a,b]	28 (58.3 %)[a]	11 (47.8 %)[b]	0.003*
Mild (n, %)	21 (19.4 %)	3 (8.1 %)[b]	8 (16.7 %)[c]	10 (43.5 %)[b,c]	0.003*
Moderate (n, %)	7 (6.5 %)	1 (2.7 %)	6 (12.5 %)	0 (0 %)	0.069
Severe (n, %)	4 (3.7 %)	0 (0 %)	3 (6.3 %)	1 (4.3 %)	0.313
Extremely Severe (n, %)	5 (4.6 %)	1 (2.7 %)	3 (6.3 %)	1 (4.3 %)	0.741
DASS-21 Stress Score	3 (0-15)	2.5 (0-6)	3 (0-15)	3 (1-13)	0.133
DASS-21 Stress					
Normal (n, %)	98 (90.7 %)	36 (97.3 %)	40 (83.3 %)	22 (95.7 %)	0.058
Mild (n, %)	4 (3.7 %)	0 (0 %)	4 (8.3 %)	0 (0 %)	0.075
Moderate (n, %)	2 (1.9 %)	0 (0 %)	2 (4.2 %)	0 (0 %)	0.280
Severe (n, %)	2 (1.9 %)	0 (0 %)	1 (2.1 %)	1 (4.3 %)	0.472
Extremely Severe (n, %)	2 (1.9 %)	1 (2.7 %)	1 (2.1 %)	0 (0 %)	0.742
Impact of Events Total Score (IES-R)	14 (1-66)	13 (1-32)[b]	13 (4-66)[c]	20 (5-58)[b,c]	0.024*
IES-R Intrusion Score	4 (0-25)	3 (0-10)[a,b]	5 (0-25)[a]	7 (0-20)[b]	0.010*
IES-R Avoidance Score	7 (0-27)	7 (0-16)	5 (1-27)	10 (2-22)	0.078
IES-R Hyperarousal Score	2 (0-17)	2 (0-10)[a,b]	3 (0-17)[a]	3 (0-16)[b]	0.024*

DASS-21 Depression, Anxiety and Stress Scale, IES-R Impact of Event Scale-Revised
*If there is p<0.05 as the significance level, P[a]:,control vs home recovery, P[b]: control vs hospital recovery, P[c]: home recovery vs hospital recovery

Table 3. Correlation of LVGLS with total DASS-21 and IES-R scores and subscale scores.

LVGLS	Variable	r	p
	Total DASS-21 Score	-0.251	0.020*

DASS-21 Depression Score	-0.168	0.119
DASS-21 Anxiety Score	-0.285	0.008*

		Total patients	Patients with	Patients with severe

DASS-21 Stress Score	-0.178	0.098
IES-R Total Score	-0.291	0.007*
IES-R Intrusion Score	-0.367	0.001*
IES-R Avoidance Score	-0.196	0.069
IES-R Hyperarousal Score	-0.188	0.081

Abbreviations: LVGLS left ventricular global longitudinal strain, DASS-21 Depression, Anxiety and Stress Scale, IES-R Impact of Event Scale-Revised

				comorbidity		pneumonia	
LVGLS	**Variable**	**r**	**p**	**r**	**p**	**r**	**p**
	Total DASS-21 Score	-0.251	0.020*	-0.232	0.139	-0.366	0.135
	DASS-21 Depression Score	-0.168	0.119	-0.232	0.140	-0.461	0.054
	DASS-21 Anxiety Score	-0.285	0.008*	-0.195	0.215	-0.203	0.419
	DASS-21 Stress Score	-0.178	0.098	-0.211	0.174	-0.485	0.041*
	IES-R Total Score	-0.291	0.007*	-0.495	0.001*	-0.716	0.002*
	IES-R Intrusion Score	-0.367	0.001*	-0.470	0.002*	-0.666	0.004*
	IES-R Avoidance Score	-0.196	0.069	-0.341	0.027*	-0.462	0.054
	IES-R Hyperarousal Score	-0.188	0.081	-0.419	0.006*	-0.500	0.041*

Table 4. Correlation of LVGLS with total DASS-21 and IES-R scores and subscale scores according to subgroups.

Abbreviations: LVGLS left ventricular global longitudinal strain, DASS-21 Depression, Anxiety and Stress Scale, IES-R Impact of Event Scale-Revised

Table 5. Correlation of conventional echocardiographic parameters with total DASS-21 and IES-R scores and subscale scores.

		LVEDV	**LVESV**	**LVEF**	**LAVI**	**LV Mass Index**	**E/A**	**E/e'**
Total DASS-21 Score	r	-0.027	-0.004	-0.019	-0.095	0.102	-0.103	0.056
	p	0.787	0.967	0.850	0.378	0.330	0.302	0.571

DASS-21 Depression Score	r	-0.128	-0.036	-0.069	-0.064	-0.002	-0.003	-0.041
	p	0.194	0.719	0.487	0.550	0.986	0.976	0.680
DASS-21 Anxiety Score	r	-0.027	-0.034	-0.003	-0.264	0.013	-0.133	0.137
	p	0.787	0.730	0.978	0.013*	0.904	0.180	0.168
DASS-21 Stress Score	r	-0.044	-0.012	0.021	-0.017	0.105	-0.123	0.053
	p	0.656	0.901	0.828	0.876	0.312	0.211	0.593
IES-R Total Score	r	0.047	0.047	-0.025	-0.135	0.079	-0.149	0.033
	p	0.637	0.636	0.798	0.216	0.459	0.136	0.745
IES-R Intrusion Score	r	0.046	0.051	-0.029	-0.059	0.029	-0.156	0.043
	p	0.646	0.607	0.767	0.586	0.786	0.116	0.671
IES-R Avoidance Score	r	0.045	0.017	0.023	-0.125	0.085	-0.111	0.067
	p	0.647	0.866	0.819	0.246	0.419	0.264	0.504
IES-R Hyperarousal	r	-0.045	0.027	-0.114	-0.263	0.092	-0.055	0.071
Score	p	0.649	0.781	0.248	0.027*	0.380	0.580	0.474

Abbreviations: DASS-21: Depression, Anxiety and Stress Scale, IES-R: Impact of Event Scale-Revised, LVEDV: Left ventricular end-diastolic volume, LVESV: Left ventricular end sistolic volume, LVEF: Left ventricular ejection fraction, LAVI: Left atrium volume index

Table 6. Correlation of LVGLS with socio-demographic characteristics.

LVGLS	**Variable**	**r**	**p**
	Age	-0.329	0.005*
	Sex[†]	-0.213	0.044*
	BMI	-0.461	<0.001*
	Educational Level	0.381	<0.001*
	Marital Status	-0.273	0.010*

Home Arrangement	-0.027	0.803
Anxiety about re-infection	-0.169	0.186
Informed about COVID	0.131	0.219

Abbreviations: LVGLS left ventricular global longitudinal strain, BMI body mass index
†: in favour of female sex

Table 7. Multivariate linear regression analysis as a predictor of LVGLS.

Variable	**β**	**95 % Confidence Interval**	**p-value**
Age	0.002	-0.100 to 0.104	0.964
Sex	-1.261	-2.778 to 0.256	0.102
Educational Level	1.432	0.350 to 2.514	0.010*
Marital Status	-0.897	-2.573 to 0.779	0.289
DASS-21 Anxiety Score	0.146	-0.059 to 0.351	0.160
Total DASS-21 Score	-0.186	-0.354 to -0.018	0.030*

Abbreviations: LVGLS left ventricular global longitudinal strain, DASS-21 Depression, Anxiety and Stress Scale.