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The Impact of Left Ventricle Geometry Patterns on Length of Hospital Stay in COVID-19 Patients

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ABSTRACT

Objective: The coronavirus disease 2019 (COVID-19) has placed huge strains on medical systems. Therefore, it is essential to determine the predictors of the long hospital stay. We sought to investigate whether alterations in left ventricular (LV) geometry in COVID-19 patients are associated with the length of stay (LoS) and a long hospital stay.

Materials and Methods: 108 consecutive hospitalized COVID-19 patients were incorporated in the study and 89 patients remained for statistical analysis. All participants underwent standard two-dimensional (2D) and Doppler echocardiographic examinations. Patients were classified according to LV geometry characteristics namely normal geometry (NG), concentric remodeling, concentric hypertrophy and eccentric hypertrophy.

Results: Multiple binary logistic regression model adjusted for clinical and laboratory variables yielded significant and independent association of LV mass index (LVMI) (OR: 1.12, 95% CI: 1.06–1.19, p<0.001), 10 g/m^2 increase in LVMI (OR: 3.63, 95% CI: 2.00–6.59, p<0.001), LV geometry patterns (OR: 2.92, 95% CI: 1.46–5.84, p=0.002), and altered geometric patterns compared to NG (OR: 3.97, 95% CI: 1.08–14.5, p=0.037) with long hospital stay. Correlation analysis of LVMI and LoS demonstrated significant and moderate correlation (rho=0.58, p<0.001).

Conclusion: LVMI and LV geometric patterns independently predict long hospital stays in COVID-19 patients. The significant correlation between LoS and LVMI underlies the significance of LV geometry in this infection.

Keywords: COVID-19, left ventricular geometry, left ventricular hypertrophy, SARS-CoV-2, transthoracic echocardiography

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, in other words, the coronavirus disease 2019 (COVID-19) pandemic, has substantially increased the burden on health systems around the world. Due to the large number of patients suffering from the disease, hospital systems have maximized their capacity and developed novel protocols to deal with this surge (1). The lower respiratory tract and subsequently the lungs are the primary targets of the virus and affected patients may require hospitalization for treatment and prevention of viral shedding. In critically ill patients, intensive care unit (ICU) follow-up may also be needed (2, 3).

Cardiovascular disease (CVD), particularly hypertension (HT), is a major contributor to adverse events, including death, in SARS-CoV-2 infection (4, 5). Left ventricle (LV) geometry patterns reflect adaptive remodeling of LV to aging, CV risk factors such as HT or myocardial injury, and are classified as normal geometry (NG), concentric remodeling (CR), concentric hypertrophy (CH), and eccentric hypertrophy (EH) (6). Impairments in LV geometry are closely linked to impaired systolic and diastolic functions (7) and mortality (8). There is a lack of research on the impact of LV geometric features on the duration of hospital stay in COVID-19. Besides, it is essential to grasp predictors of the long hospital stay in this patient group because of the increasing demand for healthcare in hospitals. A recent study also proved the prognostic utility of transthoracic echocardiography (TTE) in COVID-19 patients (9). Thus, we sought to investigate whether alterations in LV geometry are related to the length of hospital stay (LoS) and long hospital stay in COVID-19 patients.

MATERIALS and METHODS

Study Protocol and Definitions

108 consecutive COVID-19 patients hospitalized at our tertiary center hospital between May and June 2020 were included to study. Identification of SARS-CoV-2 infection was performed in line with the interim guidance report published by the World Health Organization (WHO) (10). Viral infection of SARS-CoV-2 was demonstrated by ribonucleic acid sampling in throat swap samples via polymerase chain reaction (PCR) testing. Additionally, multidetector computed tomography (CT) was performed in all hospitalized patients to examine the lungs. The discharge

criteria were the absence of fever for at least 3 days, improvement of symptoms, and two negative PCR tests taken at least 24-hour intervals. The study design and applied procedures were consistent with the Helsinki Declaration, and all study patients signed written informed consent. The hospital local ethics committee (Name: Ankara City Hospital Ethics Committee; Number: E1/20/611; Approval Date: 21/05/2020) and the Republic of Türkiye Ministry of Health also approved the study protocol. Patients with severe valvular disease (n=4), prosthetic valve (n=2), severe heart failure (n=4), previous myocardial infarction (n=3), history of coronary artery bypass graft (n=4), hypertrophic cardiomyopathy (n=1), and history of myopericarditis (n=1) were excluded from the study. Patients in severe or critical conditions according to the clinical classification proposed by the WHO-China Joint Mission report (11), or patients followed up with invasive mechanical ventilation prior to enrollment, were not included in the study. Due to the worsening of the clinical condition, 4 patients were transferred to ICU and no death occurred during the follow-up process.

Patient follow-up was performed by physicians blinded to the study protocol. Patients' basal characteristics, including comorbidities, drug use, laboratory parameters, chest CT findings, and echocardiographic calculations were obtained and recorded on a chart. The clinical status of the patients, including the decision to be discharged or referred to the ICU, were also followed up daily. Medical treatment of patients included antiviral, antibiotic therapy, and heparin, individually.

Body mass index (BMI) value was obtained by dividing the weight in kilograms by the square of height in meters and body surface area (BSA) value was obtained using the Mosteller formula (12). Patients with a BMI value below 18.5 were defined as underweight, between 18.5 and 24.9 as normal, and between 25.0–29.9 as overweight. Patients with a BMI ≥30 were defined as obese (13). Patients using hypoglycemics agents or patients with fasting glucose levels≥126 mg/dL or patients with non-fasting glucose ≥200 mg/dL were diagnosed as diabetes mellitus (DM). Repeated measures of antihypertensive medication use or mean office blood pressure measurements ≥140 mmHg for systolic and/or ≥90 mmHg for diastolic blood pressure were defined as arterial HT. A long hospital stay was defined as hospitalization of more than 10 days (14).

Laboratory Procedure

Peripheral venous blood samples were obtained from all patients immediately upon their admission to the hospital. at hospital admission immediately. Blood count tests and biochemical examinations, including D-dimer, alanine aminotransferase (ALT), creatinine, N-terminal prohormone of brain natriuretic peptide (NT-proBNP), cholesterol panel, C reactive protein (CRP), ferritin and high sensitivity troponin-I (hs-TnI) were determined by standard methods.

Transthoracic Echocardiography

All study participants underwent standard two-dimensional (2D) and Doppler echocardiographic examinations at the time of admission decision Examinations were carried out by two TTE researchers blinded to patients' clinical information and study protocol using a commercially available device (Philips iE33 xMatrix, Philips Healthcare, Inc., Andover, MA). All examinations were performed at the left lateral decubitus position, adhering to a focused, time-efficient protocol using protective equipment provided for both the patient and the echocardiographer in a echocardiography laboratory dedicated for COVID-19 patients during the pandemic. All images were recorded and analyzed subsequently to minimize viral contamination. All echocardiographic procedures were compatible with the recommendations of the American Society of Echocardiography (15). LV end-diastolic diameter (LVEDd), LV end-systolic diameter (LVESd), interventricular septum diameter (IVSd), and posterior wall thickness (PWT) were calculated from the parasternal long-axis view. Relative wall thickness (RWT) was calculated using the formula: (2xPWT)/LVEDd. Increased RWT was defined as >0.42. LV ejection fraction (LVEF) was obtained by modified 2D biplane method of disks summation technique. LV mass (LVM) was derived through the Devereux formula (16). Subsequently, LV mass index (LVMI) value was obtained by dividing LVM by BSA. LVMI values >115 g/m^2 and >95 g/m^2 for men and women, respectively, were described as increased LVMI.

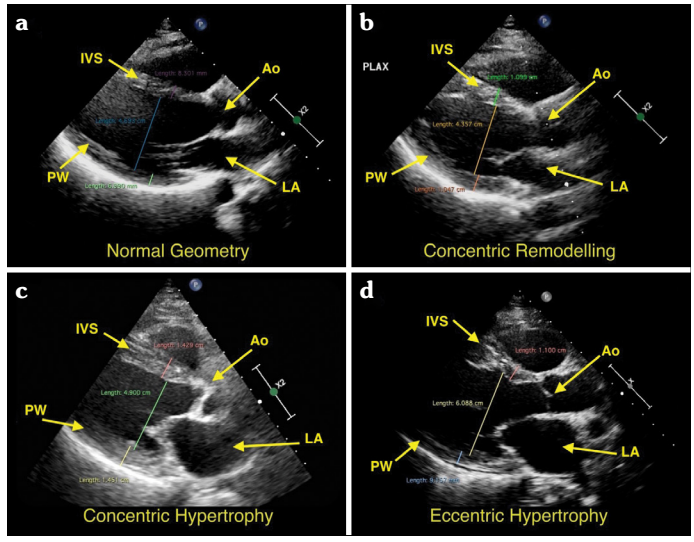


Figure 1. TTE parasternal long axis views demonstrating various left ventricular geometry patterns. (a) 52-year-old male patient with normal LV geometry. LVEDd 47 mm; IVSd 8.3 mm; PWT 7 mm; LV mass: 115 g; LV mass index 61 g/m^2; RWT 0.30. (b) 61-year-old male patient with concentric remodeling. LVEDd 44 mm; IVSd 11 mm; PWT 10.5 mm; LV mass 164 g; LV mass index 86 g/m; RWT 0.48. (c) 52-year-old male patient with concentric hypertrophy. LVEDd 49 mm; IVSd 14 mm; PWT 14.5 mm; LV mass: 290 g; LV mass index 147 g/m^2; RWT 0.59. (d) 67-year-old female patients with eccentric hypertrophy. LVEDd 61 mm; IVSd 11 mm; PWT 9 mm; LV mass: 254 g; LV mass index 132 g/m^2; RWT 0.31

Ao: Aortic valve; IVSd: Interventricular septum diameter; LA: Left atrium; LV: Left ventricle; LVEDd: Left ventricle end-diastolic diameter; PWT: Posterior wall thickness; RWT: Relative wall thickness; TTE: Transthoracic echocardiography

LV geometric patterns were defined according to LVMI and RWT measurements. NG was described as normal LVMI with normal RWT (Fig. 1a). CR was defined as normal LVMI with enhanced RWT (Fig. 1b). CH was defined as increased LVMI and RWT (Fig. 1c), and EH (Fig. 1d) was described as increased LVMI with normal RWT (17). Finally, the participants were divided into four groups according to their LV geometry characteristics: NG (n=31), CR (n=38), CH (n=13) and EH (n=7).

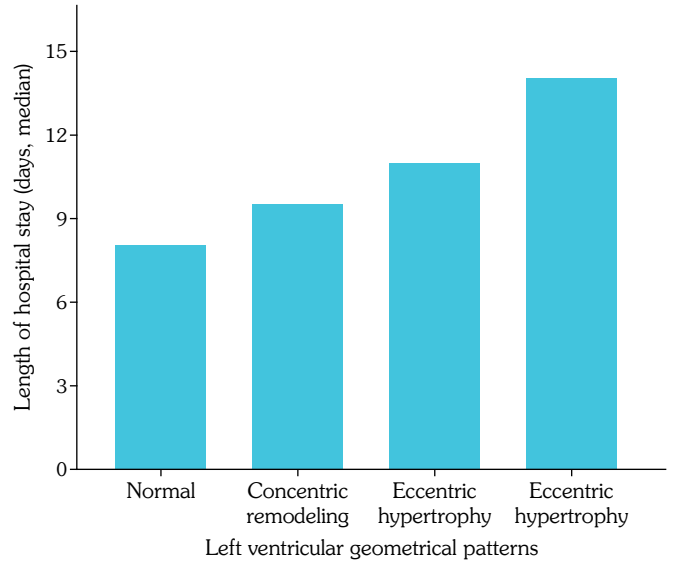
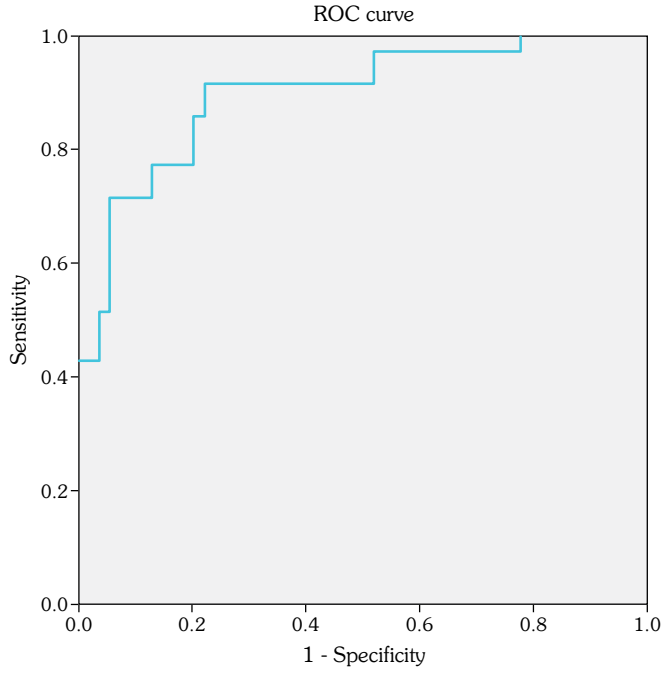


Figure 2. The association between left ventricle geometry and length of hospital stay (LoS)

Statistical Analysis

All tests were carried out through IBM SPSS Statistics for Macintosh, Version 24.0 (IBM Corp., Armonk, New York, USA). The Shapiro Wilk test was applied in order to test the distribution of continuous variables. The Chi-square test or Fisher's Exact test was performed for categorical variables. One-way analysis of variance (ANOVA) test and independent samples t-test were used for normally distributed numerical variables, while Kruskal-Wallis and Mann-Whitney-U tests were used for non-normally distributed numerical variables. Percentages were used for categorical variables, and mean±standard deviation or median with interquartile ranges (percentiles 25th and 75th) for numerical variables. The correlation of LoS with various variables, including RWT and LVMI, was determined through Spearman's correlation analysis. Multiple binary logistic regression tests were carried out to examine predictors of long hospital stay. LVMI, 10 g/m^2 increment in LVMI, LV geometry patterns, and geometric patterns varying according to normal LV geometry were investigated in four univariate and eight separate multiple models. Multiple models were adjusted for clinical features (age, gender, and HT). Furthermore, another multiple model was adjusted for clinical and laboratory features (age, HT, NT-proBNP, and lymphocyte count). The results of logistic binary regression tests were given with odds ratio (OR) and 95% confidence interval (CI), and the enter method was applied. The adjusted clinical and laboratory parameters included in the multiple analyses were selected among the variables that reached statistical significance in the comparative and correlation analyses. To avoid multicollinearity, clinical and laboratory parameters that showed significant correlations were not included in the same regression model. In addition, as few dependent variables as possible were included in the multiple analysis, which could predict the longest hospital stay at the strongest level to avoid over-adherence. Receiver operating characteristic (ROC) curve analysis was applied for calculating LVMI cut-off values that predict long hospital stays. The area under the ROC curve (AUC) was then calculated and the result was given with 95% CI, positive likelihood ratio (PLR), negative likelihood ratio (NLR), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). A two-tailed p-value less than 0.05 was defined as statistically significant.



Left ventricular mass ındex (g/m^2)	>88.8
Sensitivity, %	91.4
Specificity, %	77.8
Positive predictive value, %	72.7
Negative predictive value, %	93.3
Positive likelihood ratio	4.11
Negative likelihood ratio	0.11
Area under the curve (CI 95%)	0.89 (0.82–0.96)
p value	<0.001

Figure 3. Receiver operating characteristic (ROC) curve analyses were conducted to determine the cut-off values for the sensitivity and specificity of left ventricular mass index for predicting long hospital stay

RESULTS

After applying the exclusion criteria, the remaining 89 COVID-19 patients were incorporated in the statistical testing. The mean age of the participants was 43±16 years, and 46.1% were women with a BMI of 28.4±5.6. DM and HT were prevalent in 11.2% and 25.8% of patients, respectively. Furthermore, 4.5% of the patients had COPD.

The clinical features of the groups are presented in Table 1. Participants with NG were younger. The female gender ratio, BMI and weight status, fever and heart rate parameters, and blood pressure levels were similar between the groups. DM and HT were more

Table 1. Laboratory and echocardiographic features of the study groups according to left ventricular geometric patterns

	Normal geometry (n=31)	Concentric remodeling (n=38)	Concentric hypertrophy (n=13)	Eccentric hypertrophy (n=7)	p (overall)
Clinical features					
Age, years	33±12	49±15	47±19	46±15	<0.001
Female, n (%)	11 (35)	15 (39)	10 (76)	5 (71)	0.031
Body mass index, kg/m^2	26.3±4.4	29.4±6.1	29.0±4.9	31.5±6.3	0.052
Weight status, n (%)					0.754
Underweight	2 (6)	1 (3)	0	0	
Normal	9 (29)	8 (21)	2 (15)	1 (14)	
Overweight	13 (42)	15 (39)	5 (38)	2 (29)	
Obese	7 (23)	14 (37)	6 (46)	4 (57)	
Fever, °C	37.1 (36.9–37.3)	37.2 (36.9–37.7)	37.4 (37.1–37.8)	37.1 (36.9–37.3)	0.108
Heart rate, beats/min	73±11	82±14	81±14	75±12	0.064
Systolic blood pressure, mmHg	129 (120–134)	130 (125–134)	135 (129–138)	135 (129–138)	0.067
Diastolic blood pressure, mmHg	85 (80–87)	82 (78–89)	86 (84–88)	86 (84–88)	0.432
Diabetes mellitus, n (%)	0	5 (13)	2 (15)	3 (43)	0.010
Hypertension, n (%)	2 (6)	14 (37)	4 (31)	3 (43)	0.021
COPD, n (%)	0	3 (8)	0	1 (14)	0.199
Infiltrates present on initial chest CT	16 (52)	25 (66)	10 (64)	6 (86)	0.213
Antiviral therapy, n (%)	23 (74)	34 (89)	12 (92)	7 (100)	0.150
Antibiotic therapy, n (%)	7 (23)	14 (37)	3 (23)	5 (71)	0.070
Heparin, n (%)	28 (90)	38 (100)	13 (100)	5 (71)	0.012
Previous treatment, n (%)					
RAAS inhibitors	2 (6)	12 (32)	3 (23)	1 (14)	0.075
β-blockers	0	3 (8)	2 (15)	0	0.174
Calcium channel blockers	2 (7)	3 (8)	2 (15)	1 (14)	0.755
Diuretics	0	5 (13)	1 (8)	0	0.150
Statins	0	4 (11)	1 (8)	1 (14)	0.289
Oral antidiabetics	0	4 (11)	2 (15)	3 (43)	0.007
Lenght of hospital stay	8 (6–10)	9.5 (7.8–13.2)	11 (11–14)	14 (10–17)	<0.001
Laboratory parameters					
White blood cell, x10^9/L	5.51 (4.34–6.87)	5.40 (4.19–6.97)	4.35 (3.24–5.00)	5.11 (4.09–7.52)	0.049
Neutrophil count, x10^9/L	2.87 (2.48–4.89)	3.33 (2.13–4.61)	2.35 (1.46–2.84)	3.13 (2.39–4.39)	0.113
Lymphocyte count, x10^9/L	1.56 (1.06–2.29)	1.31 (0.97–1.77)	1.29 (1.06–1.71)	1.27 (0.68–1.39)	0.187
Platelet count, x10^9/L	235±57	243±67	230±83	231±49	0.910
Hemoglobin, g/L	14.0±1.4	13.5±1.6	13.4±1.4	12.2±1.3	0.042
Alanine aminotransferase, U/L	30 (19–39)	29 (22–39)	31 (16–62)	15 (10–26)	0.046
Creatinine, m /dL	0.82±0.21	0.81±0.23	0.80±0.23	0.76±0.17	0.938
High-density lipoprotein, mg/dL	41±15	36±11	44±8	30±7	0.048
Low-density lipoprotein, mg/dL	86±29	96±29	93±25	88±29	0.585
Triglyceride, mg/dl	121±66	124±52	122±59	117±63	0.993
D-dimer, µg/L	330 (210–460)	660 (390–1180)	610 (350–2610)	470 (360–480)	0.003
C-reactive protein, mg/L	3.8 (1.8–8.7)	15.5 (4.6–47.0)	17.0 (2.0–37.8)	10.4 (4.4–123)	0.008
Ferritin, µg/L	66 (27–127)	174 (47–314)	188 (49–283)	78 (15–195)	0.031
NT-proBNP, ng/L	26 (20–32)	35 (23–71)	58 (35–96)	45 (36–182)	<0.001
High sensitive troponin I, ng/L	2.5 (2.5–3.0)	3.0 (2.5–7.0)	3.0 (2.5–20.0)	3.0 (2.0–4.0)	0.033
2D echocardiography					
LVEDd, cm	4.82±0.37	4.40±0.45	4.70±0.28	5.20±0.14	<0.001
LVESd, cm	2.95±0.42	2.77±0.36	2.95±0.23	3.22±0.20	0.014
IVSd, cm	0.96±0.19	1.14±0.13	1.28±0.30	1.19±0.10	<0.001
PWT, cm	0.82±0.11	1.08±0.12	1.19±0.14	1.03±0.06	<0.001
RWT	0.34±0.05	0.49±0.05	0.50±0.04	0.39±0.02	<0.001
LVEF, %	58.3±6.6	60.2±5.7	60.0±5.3	55.9±3.7	0.107
LV mass, g	148 (126–148)	174 (156–199)	205 (184–235)	223 (207–252)	<0.001
LV mass index, g/m^2	77±14	89±15	121±35	115±11	<0.001

COPD: Chronic obstructive pulmonary disease; CT: Computed tomography; IVSd: Interventricular septum diameter; LV: Left ventricle; LVEDd: Left ventricle end-diastolic diameter; LVEF: Left ventricular ejection fraction; LVESd: Left ventricle end-systolic diameter; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; PWT: Posterior wall thickness; RAAS: Renin-angiotensin-aldosterone system; RWT: Relative wall thickness

prevalent in EH patients, whereas the prevalence of COPD was similar between groups. Chest CT infiltrations were also comparable between the groups. Antiviral and antibiotic therapy were at a similar rate, whereas heparin therapy significantly differed among the groups. Previous medications other than oral antidiabetics were comparable between the groups. Median values of hospital stay were 8, 9.5, 11 and 14 days for NG, CR, CH, and EH, respectively ($p<0.001$ for all) (Fig. 2). Neutrophil, lymphocyte, platelet counts, and creatinine were comparable among groups, whereas white blood cell count, hemoglobin, and ALT levels significantly differed among groups. The cholesterol panel, excluding HDL, was comparable among the groups. In addition, D-dimer, CRP, ferritin, NT-proBNP, and hs-TnI levels were differed significantly between the groups. Conventional echocardiographic measurements, including LVEDd and LVESd were higher in the EH group. Moreover, IVSd, PWT and RWT significantly differed between the groups. LVEF was comparable among groups. LVMI calculations were 77±14, 89±15, 121±35, and 115±11 g/m^2 for NG, CR, CH, and EH, respectively ($p<0.001$).

Participants were divided into two groups according to their long hospital stay status (Table 2). Patients in the long-stay group were older, had higher fever levels, DM, and HT. The presence of infiltrates on chest CT at the admission and treatments administered during hospitalization were comparable between the two groups. Previous medications of patients were similar, except for beta-blockers and diuretics. The median LoS was 14 (11–18) days in the long-stay group and 8 (6–9) days in the group without the long-stay ($p<0.001$). The lymphocyte count was significantly lower in the long-stay patient group, whereas creatinine, D-dimer, ferritin, NT-proBNP, and hs-TnI levels were significantly increased. LVEDd, LVESd, and LVEF measurements were comparable among the groups. IVSd, PWT, RWT, LVM and LVMI were significantly increased in the long-stay group. Correlation analysis revealed a significant correlation of LoS with variables such as age, fever, lymphocyte count, D-dimer, ferritin, CRP, hs-TnI, NT-proBNP, albumin, creatinine, LVMI (rho=0.58, $p<0.001$), and RWT (rho=0.25, $p=0.01$) (Appendix 1).

The association of LV hypertrophy and geometric patterns with prolong hospital stays is presented in Table 3. The multiple model adjusted for clinical variables only yielded a significant and independent association with a long hospital stay for all parameters incorporated in the model including, LVMI, 10 g/m^2 increase in LVMI, LV geometry patterns, and altered LV geometric patterns compared to NG. Furthermore, multiple model adjusted for clinical and laboratory variables also yielded significant and independent association of LVMI, 10 g/m^2 increase in LVMI, LV geometry patterns, and altered geometric patterns compared to NG with long hospital stay. ROC curve analysis for LVMI yielded an AUC 0.89 with a PLR 4.11 and NLR 0.11. The cut-off value of LVMI (88.8) was associated with 91.4% sensitivity, 77.8% specificity, PPV 72.7%, and NPV 93.3% (Fig. 3).

DISCUSSION

Our study results indicate that LVMI and LV geometric patterns detected through TTE are significant and independent predictors of the long hospital stay in patients suffering from COVID-19, and LVMI values above 88.8 can be used to predict COVID-19 patients in need of long-term hospital follow-up. Moreover, there is a significant correlation between LoS and LVMI that underlies the significance of LV geometry in COVID-19. Consequently, this is the first study in the literature demonstrating a linkage between LV geometrical features of infected patients and their length of hospital follow-up.

The COVID-19 has placed an enormous strain on local medical systems. As the pandemic continues to escalate worldwide, it is crucial to identify the predictors of prolonged hospital stays to use medical resources effectively. For example, lymphopenia and glucocorticoid treatment were linked with increased length of hospitalization in moderate or severe COVID-19 patients (18). Obesity, age, and CRP levels at admission were also found to be related to prolonged hospital stays in COVID-19 pneumonia patients (19). Besides, increased procalcitonin levels were an independent predictor of long hospital stay defined as LoS above 14 days (20). Due to the close interaction between CVD, HT and COVID-19-related adverse events (4, 5), we have hypothesized that altered LV geometry characteristics in COVID-19 patients are associated with the long hospital stays. Our multiple logistic binary regression analyses adjusted for diverse clinical and laboratory parameters revealed that LVMI, 10 g/m^2 increments in LVMI, LV geometric patterns, and altered LV geometry compared to NG features independently predicted long hospital stay. Furthermore, we found a positive and significant correlation between LoS and LVMI in the correlation analysis. TTE is a valuable tool to determine heart functions and cardiac anatomy. Besides being a non-invasive and reproducible test, it also allows for quantitative and qualitative examinations (21). For instance, LVEF, reflecting the functions of the left heart, is a strong prognostic indicator of adverse outcomes even in non-cardiac conditions (22). However, recent echocardiography studies have reported no deterioration in LVEF in most of the COVID-19 patients (23, 24), and no association with mortality (25). On the other hand, LV global longitudinal strain was found to be linked with mortality in COVID-19 patients (26). In this context, it might be reasonable to attribute a role for the left heart in COVID-19 pathogenesis, although the data supporting this statement is limited. LV remodeling, ie. alterations in LV geometry, has also been shown to predict LVEF-like adverse events as a response to various conditions (6–8) According to a previous study, changes in LV geometry characteristics, particularly CR and EH patterns, were associated with mortality as well as hospital admissions when compared with patients with NG (27). Similarly, our data demonstrated a significant and independent association between altered LV geometry and prolonged hospital stay. However, the present study did not aim to test the relationship between LV geometry characteristics and mortality in COVID-19.

Our understanding of TTE's contribution to our daily practice has changed throughout the pandemic. For example, routine and/or elective TTE examination is not recommended because of viral shedding risk and intentions to use medical resources effectively (28). However, echocardiography with safety protocols may be useful to diagnose and manage cardiac involvement in selected COVID-19 patients (29). Besides, TTE can allow for risk stratification or prediction of adverse events such as long hospital stays, as

Table 2. Clinical, laboratory and echocardiographic features of the study groups according to the long hospital stay

	Long hospital stay (+) (n=35)	Long hospital stay (-) (n=54)	p
Clinical features			
Age, years	51.4±17.6	37.6±13.2	<0.001
Female, n (%)	17 (49%)	24 (44%)	0.703
Body mass index, kg/m^2	29.8±5.4	27.5±5.6	0.061
Weight status, n (%)			0.348
Underweight	0 (0)	3 (6%)	–
Normal	6 (17%)	14 (26%)	–
Overweight	15 (43%)	20 (37%)	–
Obese	14 (40%)	17 (31%)	–
Fever, °C	37.4 (37.0–37.8)	37.1 (36.9–37.3)	0.031
Heart rate, beats/min	80.5±14.3	76.9±12.5	0.223
Systolic blood pressure, mmHg	132 (125–135)	129 (122–134)	0.276
Diastolic blood pressure, mmHg	84 (77–88)	83 (80–87	0.631
Diabetes mellitus, n (%)	7 (20%)	3 (6%)	0.035
Hypertension, n (%)	14 (40%)	9 (17%)	0.014
COPD, n (%)	1 (3%)	3 (%6)	0.548
Infiltrates present on initial chest CT	25 (71%)	32 (59%)	0.243
Antiviral therapy, n (%)	33 (94%)	43 (80%)	0.056
Antibiotic therapy, n (%)	15 (43%)	14 (26%)	0.096
Heparin, n (%)	33 (94%)	51 (94%)	0.975
Previous Treatment, n (%)			
RAAS inhibitors	10 (29%)	8 (15%)	0.115
β-blockers	5 (14%)	0 (0%)	0.004
Calcium channel blockers	4 (11%)	4 (7%)	0.517
Diuretics	5 (15%)	1 (2%)	0.020
Statins	4 (11%)	2 (4%)	0.156
Oral antidiabetics	6 (17%)	3 (6%)	0.077
Length of hospital stay, days	14 (11–18)	8 (6–9)	<0.001
Laboratory features			
White blood cell, x10^9/L	4.83 (3.95–5.54)	5.63 (4.21–6.97)	0.093
Neutrophil count, x10^9/L	2.81 (2.10–3.83)	3.07 (2.19–4.84)	0.255
Lymphocyte count, x10^9/L	1.19 (0.90–1.48)	1.49 (1.11–2.17)	0.005
Platelet count, x10^9/L	235±74	239±58	0.826
Hemoglobin, g/L	13.5±1.4	13.6±1.6	0.878
Alanine aminotransferase, U/L	29 (19–42)	29 (18–38)	0.847
Creatinine, m/dL	0.88±0.24	0.76±0.19	0.016
High-density lipoprotein, mg/dL	36.9±10.2	38.8±13.6	0.482
Low-density lipoprotein, mg/dL	97.5±27.7	87.8±28.4	0.140
Triglyceride, mg/dl	124.3±58.1	120±58.2	0.786
D-dimer, µg/L	0.61 (0.35–1.03)	0.39 (0.27–0.76)	0.034
C-reactive protein, mg/L	17.0 (4.4–28.0)	5.5 (2.9–19.5)	0.105
Ferritin, µg/L	170 (78–300)	79 (25–192)	0.015
NT-proBNP, ng/L	54 (35–116)	27 (21–36)	<0.001
High sensitive troponin I, ng/L	4.0 (2.5–9.0)	2.5 (2.5–4.0)	0.002
2D echocardiography			
LVEDd, cm	4.78±0.36	4.58±0.49	0.031
LVESd, cm	2.99±0.32	2.83±0.39	0.036
IVSd, cm	1.23±0.22	1.0±0.17	<0.001
PWT, cm	1.12±0.15	0.93±0.16	<0.001
RWT	0.47±0.07	0.41±0.09	0.003
LVEF, %	58±7	60±6	0.281
LV mass, g	203 (188–223)	154 (129–175)	<0.001
LV mass index, g/m^2	109±26	80±15	<0.001

COPD: Chronic obstructive pulmonary disease; CT: Computed tomography; IVSd: Interventricular septum diameter; LV: Left ventricle; LVEDd: Left ventricle end-diastolic diameter; LVEF: Left ventricular ejection fraction; LVESd: Left ventricle end-systolic diameter; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; PWT: Posterior wall thickness; RAAS: Renin-angiotensin-aldosterone system; RWT: Relative wall thickness

Table 3. Univariate and multiple binary logistic regression analyses evaluating predictors of longer length of hospital stay

		Univariate		Multiple clinical* features		Multiple clinical* and laboratory† features	
		OR (95% CI)	p	OR (95%CI)	p	OR (95%CI)	p
LV mass index		1.13 (1.07–1.19)	<0.001	1.13 (1.07–1.19)	<0.001	1.12 (1.06–1.19)	<0.001
LV mass index in 10 g/m^2 increments		3.83 (2.20–6.67)	<0.001	3.81 (2.12–6.84)	<0.001	3.63 (2.00–6.59)	<0.001
Left ventricle geometry patterns		3.47 (1.92–6.27)	<0.001	3.63 (1.73–7.59)	0.001	2.92 (1.46–5.84)	0.002
Concentric remodeling	compared to						
Concentric hypertrophy	Normal geometry	7.75 (2.40–24.9)	<0.001	4.52 (1.27–15.9)	0.019	3.97 (1.08–14.5)	0.037
Eccentric hypertrophy							

*: Adjusted to basal characteristic and clinical features including age, gender and hypertension; †: Adjusted to basal characteristic and laboratory features including; age, hypertension, NT-proBNP and lymphocyte count; LV: Left ventricle; OR: Odds ratio; CI: Confidence interval

proven in our study. At this point, one can suggest applying a biomarker-based strategy instead of cardiac imaging. Various cardiovascular biomarkers such as troponin, BNP, D-dimer, prothrombin time, platelet counts, angiotensin II, etc. have been identified during the pandemic, with inherent advantages and disadvantages (30). On the other hand, TTE examination may help to determine anatomical and functional deteriorations in COVID-19 patients (30). For example, a recent study conducted with COVID-19 patients demonstrated that the presence of cardiac injury with echocardiographic abnormalities independently predicts in-hospital death (9). In light of the results obtained from this study and our analyses, it is reasonable to conclude that TTE examination might be useful in COVID-19 patients and should be considered for identification and/or prognostic evaluation of high risk patients.

Limitations

There are numerous limitations that should be underlined. First, the relatively small sample size and single-center design might limit the interpretation of these findings. Second, our study cohort included non-critically ill COVID-19 patients followed up in the service. Therefore, these findings are unpredictable for all COVID-19 patient populations, underlining the need for future studies with randomized larger patient groups in a variety of clinical situations. In addition, the limited accuracy of LVM measurement through 2D echocardiography should be kept in mind. Although we did not evaluate the hemodynamic status of the patients, it is not possible to distinguish the effects of hemodynamic factors including preload, afterload, contractility, and systemic vascular resistance in LV geometric patterns.

CONCLUSION

LVMI and LV geometric patterns significantly and independently predict long hospital stay in COVID-19 patients. The significant correlation between LoS and LVMI underlies the significance of LV geometry in COVID-19. TTE examination might be useful and should be considered in COVID-19 patients.

Ethics Committee Approval: The Ankara City Hospital Clinical Research Ethics Committee granted approval for this study (date: 21/05/2020, number: E1/20/611).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Appendix 1. Significant correlation between lenght of hospital stay and other variables

Variables	Length of hospital stay, days rho coefficient*	p
Age	0.450	<0.001
Fever	0.227	0.032
Lymphocyte count	-0.352	0.001
D-dimer	0.248	0.019
Ferritin	0.332	0.001
C- reactive protein	0.268	0.011
Troponin I	0.356	0.001
NT- proBNP	0.437	<0.001
Albumin	-0.379	<0.001
Creatinine	0.244	0.021
Left ventricular mass index	0.580	<0.001
Relative wall thickness	0.250	0.018

*: Spearman's rho co-efficient