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Evaluation of Right Ventricular Global Longitudinal Strain in COVID-19 Patients After Intensive Care Unit Discharge

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Abstract

Background and Aim: Using two-dimensional speckle tracking echocardiography (2D-STE), the ventricular functions of hospitalized coronavirus disease-2019 (COVID-19) patients were assessed. However, there is limited information about cardiac functions in the first year after recovery from the intensive care unit (ICU). This research aims to assess the right ventricular functions of COVID-19 patients and their changes within the first year after ICU discharge using 2D-STE.

Materials and Methods: The study was conducted prospectively. The study included 68 consecutive patients and 70 control patients. Echocardiography was performed in the ICU and the first year after discharge from the hospital. Right ventricular global longitudinal strain (RVGLS) was measured using the 2D-STE method.

Results: The mean age of the study group was 48.67 ± 8.10 and 37 (54.4%) patients were males. There were no substantial differences across the groups, including age, gender, body mass index, heart rate, diabetes, dyslipidemia, and smoking ($P > 0.05$). A substantially significant positive correlation was detected between right ventricular dimension (RAD) ($r = 0.644$, $P < 0.001$), right ventricular diastolic dimension (RVDD) ($r = 0.573$, $P < 0.001$), ferritin ($r = 0.454$, $P < 0.001$), D-dimer ($r = 0.305$, $P = 0.011$) values and RVGLS in the in-hospital and after-discharge first-year groups. The RVGLS values of the control, in-hospital, and after-discharge first-year groups were -20.36 ± 3.06 , -16.98 ± 3.78 , and -17.58 ± 6.45 , indicating a statistically significant difference across the groups ($P < 0.001$). Tricuspid annular plane systolic excursion was higher in the control group ($P < 0.05$).

Conclusion: RVGLS was found to be depressed during the in-hospital period and showed no improvement in the 1 year post discharge.

Keywords: Echocardiography, strain, right ventricle, speckle-tracking, COVID-19

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INTRODUCTION

Coronavirus disease-2019 (COVID-19), which has turned into a widespread epidemic worldwide, first affects the respiratory system.^[1] Although we know that it directly affects the heart, it usually causes cardiac impairment secondary to the involvement of other organs.^[2] Recent investigations have revealed that the cardiac involvement may result in pericarditis, myocarditis, cardiac tamponade, and myocardial infarction.^[3] The most common cause of in-hospital mortality in COVID-19 patients is ventricular dysfunction.^[4]

The right ventricle (RV) is more likely to be damaged than the left ventricle (LV) due to rising RV afterload because COVID-19 primarily affects the lungs.^[5] In previous research, individuals with acute respiratory distress syndrome (ARDS) and respiratory failure were found to have RV dysfunction.^[6] Standard echocardiographic measures may not be able to detect subclinical RV abnormalities, which makes diagnosis and risk categorization difficult. The most objective and sensitive examination of RV systolic dysfunction is provided by two-dimensional speckle tracking echocardiography (2D-STE).^[7] Thus, right ventricular global longitudinal strain (RVGLS) has been examined for predicting mortality in hospitalized patients. In COVID-19 patients, evaluation of RV function with 2D-STE in the first year after intensive care unit (ICU) discharge has not been published.

This study aims to investigate whether improving RV functions or not by measuring RVGLS with 2D-STE at the end of the first year after discharge from the ICU.

MATERIALS AND METHODS

The selection of participants

The study was conducted prospectively. The RVGLS values of 68 consecutive patients who met the inclusion criteria from COVID patients admitted to the critical care unit between December 2020 and December 2021 were recorded, and RVGLS values were reanalyzed after a 1 year follow-up between December 2021 and December 2022. The study included 70 healthy volunteers as a control group. Clinical conditions affecting RV strain such as structural heart disease, hypertension, chronic liver or kidney disease, pulmonary embolism, malignancy, history of asthma and pulmonary hypertension, obstructive pulmonary disease, and previous COVID were excluded from the study. Additionally, patients who had COVID of within the first year after discharge and who died were not included in the study.

Study protocol

Demographic characteristics, echocardiographic measurements, and blood samples of patients with COVID-19 hospitalized in

intensive care were obtained from medical records. Complete blood cell analysis, C-reactive protein (CRP), ferritin, hs-TnT, D-dimer, and echocardiography were performed for all patients in the first year after discharge. Blood samples were examined from the control group while echocardiography was performed on the same day. All patients underwent bedside transthoracic echocardiographic tests using the Philips EPIQ 7C device (Andover, Massachusetts). The size of the right atrium and RV was assessed using a 4-chamber apical view. On M-mode imaging, tricuspid annular plane systolic excursion (TAPSE) was measured as the systolic displacement of the tricuspid lateral annulus. Using PW tissue Doppler imaging, the RV myocardial performance index (RVMPI) was measured. (RV end-diastolic area RV end-systolic area)/end-diastolic area 100% was used to determine RV fractional area change (RVFAC). Pulmonary artery systolic pressure (sPAP) was measured using the peak velocity of the tricuspid regurgitation jet and the size and collapsibility of the inferior vena cava to calculate right atrial pressure.^[8] In line with recommendations from the American Society of Echocardiography and the European Association of Cardiovascular Imaging^[9], 2D-STE was applied to assess longitudinal systolic strain (Figure 1). Images were obtained in the four (4C)-chamber views at 70-100 frames per second from the end of expiration and were evaluated blindly by two independent specialists.

Ethical statement

This study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital (no: 133, date: 22.07.2022). It adhered to the Declaration of Helsinki's ethical guidelines for human experimentation (2013).

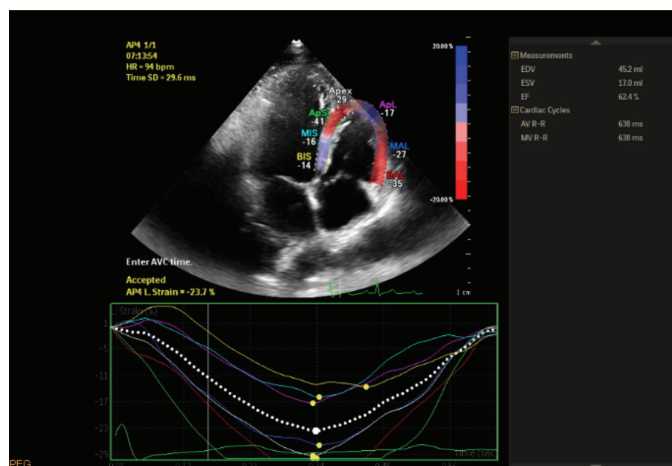


Figure 1: Measurement of right ventricular global longitudinal strain

Statistical analysis

IBM SPSS 24.0 version analyzed the data. Student's t-test or One-Way analysis of variance was used for normally distributed data and Mann-Whitney U or Kruskal-Wallis tests was used for non-normally distributed data. The chi-square or Fisher's exact test was used to compare categorical variables reported as frequency (%). The correlation between RVGLS and right ventricular dimension (RAD), RVDD, TAPSE, sPAP, D-dimer, CRP, and ferritin levels was determined using Pearson or Spearman correlation analysis. A $P < 0.05$ signified statistical validity.

RESULTS

A total of 138 individuals, 68 of whom recovered from COVID-19 and 70 controls, were enrolled in the study. The average age of the study group was 48.67 ± 8.10 and 37 (54.4%) patients were male. There were no substantial differences across the groups,

including age, gender, BMI, HR, diabetes, dyslipidemia, and smoking ($P > 0.05$, Table 1).

The WBC, CRP, D-dimer, and ferritin levels were higher in the study group than in the controls ($P < 0.001$). In the study group, 7 (10.3%) patients had ARDS, and 6 (8.8%) patients were administered immune-modulators. High-flow oxygen was given to 9 (13.2%) patients. Non-invasive mechanical ventilation and IMV were performed on 16 (23.5%) and 7 (10.3%) patients, respectively. In the echocardiographic parameters, RAD, RVSD, RVDD, RVMPI, RVGLS, and sPAP were higher in the in-hospital and after-discharge first-year groups ($P < 0.05$, Table 2). E/A ratio was lower and LV ejection fraction was higher in the control group ($P > 0.05$).

The RVGLS values of the control, in-hospital, and after-discharge first-year groups were -20.36 ± 3.06 , -16.98 ± 3.78 , and -17.58 ± 6.45 , indicating a statistically significant difference across the

Table 1: Clinical characteristics and laboratory parameters of patients

Parameters	The control group <i>n</i> = 70	The study group <i>n</i> = 68	<i>P</i> -value
Age (years)	47.24±8.45	48.67±8.10	0.311
Gender, male, n (%)	33 (47.1)	37 (54.4)	0.393
BMI (kg/m ²)	23.67±4.24	24.31±4.54	0.396
HR (beats/min)	86.0±8.75	89.2±13.23	0.092
Diabetes mellitus, n (%)	15 (21.4)	19 (27.9)	0.375
Dyslipidemia, n (%)	6 (8.6)	8 (11.8)	0.534
Smoking, n (%)	19 (27.1)	16 (23.5)	0.626
Laboratory findings			
Hemoglobin (g/dL)	13.67±2.03	13.09±2.40	0.124
WBC (10 ³ /μl)	8.26±0.77	11.93±4.23	<0.001
Lymphocytes (10 ³ /μl)	2.84±0.78	2.79±1.48	0.238
Neutrophil (10 ³ /μl)	6.02±7.89	6.35±1.48	0.094
Increased troponin, n (%)	-	22 (32.4)	-
Glucose (mg/dL)	88.45±8.56	92.29±23.28	0.199
CRP (mg/L)	0.3 (0.08)	2.1 (2.51)	<0.001
D-dimer (ng/mL)	238.5 (20.0)	810 (260.2)	<0.001
Ferritin (mL/ng)	181.5 (35.5)	495.5 (31.2)	<0.001
ALT (U/L)	21.54±8.33	21.89±8.63	0.807
AST (U/L)	23.68±5.22	24.51±9.61	0.529
Treatment			
Immune modulator, n (%)	-	6 (8.8)	-
Highflow, n (%)	-	9 (13.2)	-
NIMV, n (%)	-	16 (23.5)	-
IMV, n (%)	-	7 (10.3)	-
ARDS, n (%)	-	7 (10.3)	-
Data are expressed as appropriate as mean ± standard deviation and median (interquartile range). BMI: Body mass index, HR: Heart rate, WBC: White blood cell, CRP: C-reactive protein, ALT: Alanine transaminase, AST: Aspartate transaminase, NIMV: Non-invasive mechanical ventilation, IMV: Invasive mechanical ventilation, ARDS: Acute respiratory distress syndrome			

groups ($P < 0.001$). RVFAC was not significant across the groups ($P > 0.05$). TAPSE was higher in the control group ($P < 0.05$). There were no significant differences between the in-hospital and after-discharge first years in terms of echocardiographic parameters ($P > 0.05$). However, sPAP was statistically different between the in-hospital and after-discharge first-year groups ($P = 0.031$). On the other hand, RVSD and RVMPI were statistically significant between the in-hospital and control groups ($P = 0.044$, $P = 0.048$). There was an association between RVGLS and RAD, RVDD, TAPSE, sPAP, D-dimer, CRP, and ferritin levels. A positive correlation was detected between RAD ($r = 0.644$, $P < 0.001$), RVDD ($r = 0.573$, $P < 0.001$), ferritin ($r = 0.454$, $P < 0.001$), D-dimer ($r = 0.305$, $P = 0.011$) values and the in-hospital group. Likewise, a negative correlation was detected between TAPSE ($r = -0.511$, $P < 0.001$), CRP ($r = -0.315$, $P = 0.009$) and the in-hospital group (Table 3).

In addition, a positive correlation was determined between RAD ($r = 0.409$, $P = 0.001$), RVDD ($r = 0.268$, $P = 0.027$), Ferritin ($r = 0.495$, $P < 0.001$), D-dimer ($r = 0.388$, $P = 0.001$) and after-discharge first-year group.

DISCUSSION

This study evaluated right ventricular functions with 2D-STE in the first year in ICU discharge. After one year of follow-up, no statistically significant RV improvement was observed in RAD, RVSD, RVDD, TAPSE, and RVGLS parameters ($P > 0.05$). On the contrary, the sPAP value increased even more ($P = 0.031$).

Viral infections provoke an intense inflammatory reaction in the body. CRP, ferritin, and D-dimer were indicators of the systemic inflammation of COVID-19. CRP was found to be high in 75-90% of patients with severe COVID-19 involvement.^[10] A value greater than 10 indicates the widespread involvement. In Chinese studies by Guan et al.^[11], 46% of individuals had raised D-dimer values (>0.5 mg/L). Huang et al.^[12] discovered that COVID-19 hospitalized in the ICU had a greater D-dimer level than those who did not receive ICU care. Another acute phase reactant is serum ferritin.^[13] In Zhou et al.^[14] retrospective research, blood ferritin levels were significantly higher in non-survivors than in survivors. Mahmoud-Elsayed et al.^[15] reported that inflammation parameters predicted RV dysfunction independently of left ventricular dysfunction in patients with

Table 2: Comparison of right ventricular echocardiographic parameters between the groups

	The control group (A) <i>n</i> = 70	The study group (In-hospital) (B) <i>n</i> = 68	The study group (After discharge first year) (C) <i>n</i> = 68	P (A-B)	P (B-C)	P (A-C)
RAD (mm)	3.59±0.45	3.81±0.72	3.70±0.67	0.041	0.305	0.022
RVSD (mm)	2.77±0.50	2.96±0.73	2.92±0.57	0.048	0.461	0.166
RVDD (mm)	3.75±0.59	4.01±0.74	3.81±0.55	0.019	0.072	0.049
RVFAC (%)	53.18±8.91	51.69±8.92	52.76±9.15	0.083	0.287	0.605
RVMPI	0.47±0.07	0.50±0.10	0.49±0.07	0.044	0.395	0.130
RVGLS (%)	-20.36±3.06	-16.98±3.78	-17.58±6.45	<0.001	0.453	<0.001
TAPSE (mm)	2.20±0.14	2.08±0.30	2.10±0.30	0.007	0.692	0.014
sPAP (mmHg)	17.20±4.53	26.60±7.11	24.70±3.20	<0.001	0.031	<0.001
E/A ratio	1.5±0.52	1.7±0.91	1.6±0.58	0.168	0.387	0.423
LVEF (%)	65.1±3.9	64.2±7.7	64.6±5.5	0.412	0.197	0.384

Values are mean ± standard deviation, n (%), or median (interquartile range). RAD: Right atrium dimension, RVSD: Right ventricular systolic dimension, RVDD: Right ventricular diastolic dimension, RVFAC: Right ventricular fractional area change, RVMPI: Right ventricular myocard performance index, RVGLS: Right ventricular global longitudinal strain, TAPSE: Tricuspid annular plane systolic excursion, sPAP: Systolic pulmonary artery pressure, LVEF: Left ventricular ejection fraction

Table 3: Correlation of right ventricular global longitudinal strain with parameters

		RAD	RVDD	TAPSE	sPAP	CRP	Ferritin	D-dimer
RVGLS In-hospital	<i>r</i>	0.644	0.573	-0.511	-0.200	-0.315	0.454	0.305
	<i>P</i>	<0.001	<0.001	<0.001	0.101	0.009	<0.001	0.011
RVGLS After discharge	<i>r</i>	0.409	0.268	-0.229	0.160	-0.081	0.495	0.388
	<i>P</i>	0.001	0.027	0.060	0.193	0.514	<0.001	0.001
RVGLS Controls	<i>r</i>	-0.403	-0.026	0.059	0.331	-0.011	0.072	-0.306
	<i>P</i>	0.001	0.830	0.628	0.005	0.929	0.556	0.010

RVGLS: Right ventricular global longitudinal strain, RAD: Right atrium dimension, RVDD: Right ventricular diastolic dimension, TAPSE: Tricuspid annular plane systolic excursion, sPAP: Systolic pulmonary artery pressure, CRP: C-reactive protein

COVID-pneumonia. Although these parameters were associated with mortality in many meta-analysis studies, the values were mostly associated with the severity of the disease in our study.^[16] Qeadan et al.^[17] obtained results similar to the outcomes of our study.

Right ventricular dysfunction has been reported in echocardiography of COVID-19 patients.^[18] In a large-scale study of 69 countries, Dweck et al.^[19] noted that a quarter of all patients had right ventricular dysfunction, with the vast majority of these patients exhibiting severe symptoms. The RV dilates due to an increase in afterload. This increases RAD, RVSD, and RVDD. In a meta-analysis, Corica et al.^[20] reported that 1 in 5 patients had increased right ventricular diameters. The vast majority of them consisted of ICU patients. In accordance with earlier research and Chotalia et al.'s^[21] findings, the patient's right ventricular diameters and sPAP values were found to be increased in our study.

TAPSE, RVFAC, and RVMPI are conventional measures of the right ventricular ejection fraction. According to Baycan et al.^[22] research, there was no difference in RVFAC and RVMPI between the control and study groups. Li et al.^[23] found lower TAPSE and RVFAC values lower and higher RVMPI in COVID patients compared with the control group. Günay et al.^[24] found lower RVFAC values in recovery patients. Catena et al.^[25] reported that there was no difference in right ventricular conventional parameters between the in-hospital and post-discharge groups. The same results were obtained in our study ($P > 0.05$).

Unlike conventional methods, RVGLS is an independent predictor of COVID involvement and is a superior method because it is measured independently of angle.^[26] Using the RVGLS measure, Turan et al.^[27] revealed right ventricular impairment following recovery in asymptomatic and mildly symptomatic individuals. Carluccio et al.^[28] demonstrated that this method provides prognostic information for right ventricular failure in patients with preserved TAPSE and RVMPI measurements. Ozer et al.^[29] reported that TAPSE and RVFAC values were normal in the echocardiography performed at the 3rd month after discharge from the ICU, and only deterioration in RVGLS values. In our study, although RVGLS values were lower than those in the control group, no improvement was found in RVGLS values in the first year in discharge. In addition, a correlation has been found between RVGLS and inflammatory markers.^[30] In this trial, a positive correlation was found between RVGLS measurement, which is a sensitive indicator of right ventricular subclinical involvement, and CRP, D-dimer, and ferritin. Increased CRP, D-dimer and ferritin levels at the hospital admission and to recovery were related to RVGLS impairment, supporting this conclusion.

Study limitations

Our study population was small. Previously, detailed echocardiography measurements of the patients were not available in the records. Due to technical limitations, 3D-STE and cardiac MRI were not performed on the patients.

CONCLUSION

In this study, the results showed that impaired RVGLS values did not improve at the first year of follow-up. The long-term effects of COVID-19 infection on right ventricular function are unknown, so prospective studies with longer follow-ups are required.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital (no: 133, date: 22.07.2022).

Informed Consent: Prospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.G., A.A., A.Ak., R.K., M.A.I., M.Z.K., Concept: S.G., A.A., T.G., F.K., M.Ç., M.Z.K., Design: S.G., A.Ak., R.K., B.A., M.Z.K., Data Collection or Processing: S.G., T.G., M.Z.K., Analysis or Interpretation: S.G., A.A., M.A.I., M.Ç., M.Z.K., Literature Search: S.G., A.Ak., F.K., B.A., M.Z.K., Writing: S.G., M.A.I., M.Z.K.

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