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Original article

Speckle Tracking Echocardiographic Assessment of Left Ventricular Global Longitudinal Strain in Patients Recovered from COVID-19

Abdelrahman G. Abdelrahman, Heba A. Mansour, Mohamed A. Hamouda, Safaa S. Imam

Department of Cardiology, Faculty of Medicine Benha University, Egypt.

Corresponding to: Abdelrahman G. Abdelrahman, Department of cardiology, Faculty of Medicine Benha University, Egypt.

Email:

abdogamala2@gmail.com

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ABSTRACT:

Background: The COVID-19 infection has firmly established itself as a pandemic that can affect many body systems, including the cardiovascular system.2D speckle tracking echocardiography (2D-STE) can diagnose early subclinical myocardial dysfunction, as many studies have reported an inverse correlation of increased cardiac biomarkers level with global longitudinal strain (GLS) values among COVID-19 patients. **Aim:** This study assessed the global Left ventricular strain using speckle tracking echocardiography in patients recently recovered from COVID-19 infection. **Patients and methods:** This study was done in Benha University Hospital from June 2022 to January 2023 and included 100 patients who had positive COVID-19 diagnosis proved by positive polymerase chain reaction (PCR) test of the nasopharyngeal swab within 30 ±5 days. **Results:** Patients were classified according to the upper laboratory limit of the hs-troponin (11.6) into two groups; with myocardial injury (hs-troponin > 11.6) and without myocardial injury (hs-troponin ≤ 11.6). Patients with myocardial injury had significantly lower EF and LVGLS ($P < 0.001$). No significant differences were observed regarding ECG abnormality, D-dimer, and TLC. Moreover, LVGLS showed significant negative correlations with age ($P < 0.001$), hs-troponin ($P = 0.013$), and D-dimer ($P = 0.013$). In contrast, it showed a significant positive correlation with EF ($P < 0.001$), and no significant correlation was observed with TLC ($P = 0.408$). **Conclusion:** Serial measurements of cardiac troponin and LVGLS following recovery from COVID-19 infection has an incremental prognostic value and can be used to evaluate the progression of sub-clinical LV dysfunction.

Keywords: COVID-19, myocardial injury, cardiac troponin, global longitudinal strain.

Introduction:

The COVID-19 infection, which occurs as a result of infection with the novel coronavirus SARS-CoV-2, is a highly infectious and pathogenic viral infection **(1)**. Corona viruses are enveloped, positive-stranded RNA viruses with a nucleocapsid, and the genomic structure is organized as a single stranded RNA of approximately 30 kb in length **(2).** Upon entry into the host, replication of the viral RNA starts with the synthesis of polyprotein 1a/1ab (pp1a/pp1ab). The transcription occurs

through the replication-transcription complex (RCT) organized in double-membrane vesicles and via the synthesis of sub genomic RNAs (sgRNAs) sequences **(3).** COVID-19 is considered mainly as a respiratory viral illness. The pathogenesis of COVID- 19 induced pneumonia is best explained by two stages, an early and a late phase. **(4).**The early phase is characterized mainly by viral replication resulting in direct virus-mediated tissue damage **(5)**, while the late phase occurs later when the infected host cells trigger an immune response with the recruitment of T lymphocytes, neutrophils and monocytes that release many cytokines**(6)**.However, it can affect all body systems, including the cardiovascular system. Acute myocardial injury, detected by elevated serum levels of cardiac biomarkers, heart failure, arrhythmias, myocarditis and acute coronary syndromes have been described as its common cardiovascular complications **(7)**. Recent studies have indicated that endothelial dysfunction is a main feature of COVID-19 infection. This relation is evidenced by the role of the vascular endothelium in the hyperinflammatory state, as well as multiple cardiovascular and COVID 19 related pathologies **(8)**. Also, the hypercoagulable state and disseminated intravascular coagulation observed in COVID-19 reflect a state of endothelial damage and enhances thrombosis by reduced endothelial integrity leading to exposure of prothrombotic subendothelial matrix with subsequent initiation of clotting cascades, thrombin activation, and fibrin production **(9).** Moreover, Acute viral infections including SARS, influenza and COVID-19 can trigger ACS **(10)** and may directly cause inflammation in the coronary vasculature, in addition to causing systemic inflammation **(11)**.Oxygen supply demand mismatch is considered one of the possible mechanisms of COVID-19 induced ACS, as hypoxia and respiratory failure are considered the leading causes of death in COVID-19, accounting for about 60% of cases with fatal outcome **(12)**. The severe hypoxic state, combined with other factors such as: sepsis and hypotension can induce myocardial damage due to the mismatch between oxygen supply and demand in absence of significant atherothrombotic lesions **(13).** Given their high complexity and vulnerability, critically ill patients with COVID-19 are highly susceptible to the occurrence of type 2 MI **(14).** Furthermore, myocardial infarction with nonobstructive coronary arteries (MINOCA) has been widely reported among COVID-19 patients. Several mechanisms have been proposed for these cases, including coronary vasospasm, plaque erosion and microthrombi. **(15)**. 2D speckle tracking echocardiography (2D-STE) can diagnose subclinical myocardial dysfunction earlier than conventional echocardiography **(16)**. Recent studies have reported an inverse correlation of increased cardiac biomarkers level with global longitudinal strain (GLS) values in the population **(17)**. However, the level of cardiac involvement, if any, should be identified and which patient group is more risky, So that we can determine which patient group should be followed-up and treated for long-term cardiac involvement **(18)**.

Patients and methods:

Study design:

Analytical cross section study at Benha University Hospital.

Ethical consideration:

Before doing echocardiography or taking blood samples, a written informed consent was taken from each patient.

Patients:

One hundred patients who were tested Positive for COVID 19 infection at Benha University Hospital.

Inclusion criteria:

Patients who had COVID-19 diagnosis proved by positive polymerase chain reaction (PCR) test of the nasopharyngeal swab after 30 ±5 days.

Exclusion criteria:

*Age is less than 18 years.

*Patients presented with acute coronary syndrome.

*Patients presented with acute heart failure.

*Patients presented with rapid tachyarrhythmias including atrial fibrillation and ventricular arrhythmias.

*Patients presented with venous thromboembolism (pulmonary embolism).

*Patients presented with renal failure (eGFR < 30 ml/min).

*Patients presented with severe chronic obstructive pulmonary disease (COPD).

*Patients with poor echogenicity

Methods:

a) Written informed consent:

It was taken before the start of the study. No risks will be found and any unexpected risk appearing during the study will be cleared to the patients and the committee on time.

b) Complete history taking:

Age, gender, hypertension, diabetes, smoking, dyslipidemia, history of IHD, onset and offset of COVID symptoms.

c) Clinical examination

Complete physical examination including: vital signs with general, chest, and cardiac examination.

d) 12 Lead ECG:

To detect any recent ischemic changes, tachyarrhythmias or chamber enlargement.

e) Routine lab investigations:

Serum creatinine, complete blood picture, D-dimer and high sensitive troponin (hs-TnI).

F) Echocardiography:

Echocardiographic examination was performed on patients within one month after discharge. Echocardiographic images were obtained and recorded by standard techniques. Left ventricular global longitudinal strain (LV-GLS) was analyzed by using the Qlab13 program. The mean GLS was calculated by averaging the peak GLS values of apical two-chamber, apical three-chamber, and apical four-chamber images.

G) Statistical design:

Data management and statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Kolmogorov–Smirnov test, the Shapiro-Wilk test, and direct data visualization methods. Quantitative data were compared according to myocardial injury using the independent t-test or Mann-Whitney U test for normally and non-normally distributed quantitative data. Categorical data were compared using the Chi-square test. ROC analysis was done for LVGLS to predict myocardial injury. The area under the curve with a 95% confidence interval, best cutoff point, and diagnostic indices were calculated. Correlations were done using Pearson's or Spearman's correlation. Multivariate stepwise logistic regression analysis was done to predict myocardial injury. The odds ratios with 95% confidence intervals were calculated. All statistical tests were two-sided. P values less than 0.05 were considered significant.

Research ethics committee: MD.4.6.2021

Results:

Among the studied patients, the mean age was 54 ±15 years. More than half (58%) were females. Diabetes mellitus and hypertension were reported in 41% and 52%, respectively. Half the patients had dyslipidemia (50%), and half were smokers (50%). About one-third (41%) had a history of IHD. The median time from diagnosis was 13 days, ranging from 2-27 days **(Table 1).**

Patients were classified according to the upper laboratory limit of the hs-troponin (11.6) into two groups; with myocardial injury (hs-troponin > 11.6) and without myocardial injury (hs-troponin ≤ 11.6). Patients with myocardial injury had significantly lower EF (58 ±3 vs. 63 ±1, P < 0.001) and LVGLS (-17.8 ±1.5 vs. -20.2 ±0.4, P < 0.001). No significant differences were observed regarding ECG abnormality (P = 0.292), D-dimer (P = 0.370), and TLC (P = 0.553) (Table 2)

LVGLS showed significant negative correlations with age (r = -0.709, P < 0.001), hs-troponin (r = -0.924, P < 0.001), and D-dimer (r = -0.247, P = 0.013). In contrast, it showed a significant positive correlation with EF (r = 0.894, P < 0.001). No significant correlation was observed with TLC (P = 0.408) (Table 3).

Table (1): General characteristics of the studied patients

General characteristics		
Age (years)	Mean ±SD	54 ±15
Sex		
Males	n (%)	42 (42)
Females	n (%)	58 (58)
Diabetes mellitus	n (%)	41 (41)
Hypertension	n (%)	52 (52)
Dyslipidemia	n (%)	50 (50)
Smoking	n (%)	50 (50)
History of IHD	n (%)	41 (41)
Time from COVID recovery (days)	Median (range)	13 (2 - 27)

Table (2) Clinical characteristics of the studied patients according to myocardial injury

		Myocardial injury		
		Yes (n = 76)	No (n = 24)	P-value
ECG abnormality	n (%)	56 (73.7)	15 (62.5)	0.292
EF (%)	Mean ±SD	58 ±3	63 ±1	<0.001*
LVGLS	Mean ±SD	-17.8 ±1.5	-20.2 ±0.4	<0.001*
D Dimer	Median (range)	590 (132 - 1410)	345 (273 - 1438)	0.370
TLC	Median (range)	9 (3.2 - 18.5)	7.5 (3.4 - 17.4)	0.553

Table (3) Correlation between LVGLS and other parameters

	LVGLS	
	R	P
Age (years)	-.709	<0.001*
EF %	.894	<0.001*
hs-Troponin (ng/mL)	-.924	<0.001*
D-dimer	-.247	0.013*
TLC	-0.084	0.408

Discussion:

Various studies have reported an inverse correlation of increased cardiac biomarkers level with global longitudinal strain (GLS) values among the patients with or without established cardiovascular disease. Studies in the literature had focused on the increase in cardiac troponin levels and cardiac involvement due to COVID-19 during hospitalization **(19)**.

The aim of the current study was to assess the global Left ventricular strain using speckle tracking echocardiography in patients recently recovered from COVID-19 infection.

In agreement with those results, a previous study analyzed 13 meta-analyses and examined 3027 patients with COVID-19 infection in 2020, and found that elevated troponin levels were significantly associated with disruption in the LV-GLS, and increased severity of the disease and mortality **(20)**.

Furthermore, it was shown that among 127 post COVID-19 patients included in his study in 2021, patients with myocardial injury showed significantly lower EF (p=0.032), LVGLS (p=0.05) and higher LA diameter (p=0.01). However, in contrast to our study, it was shown that patients with myocardial injury had also significantly higher levels of D Dimer and TLC (P=0.01) **(21)**.

As regard the LVGLS and its correlation with other parameters, a study done to evaluate the LVGLS among 134 patients recovered from COVID-19 infection, found that there was a significant correlation between cardiac troponins and LVGLS ($p < 0.0001$) suggesting impaired LVGLS among patients with myocardial injury during index hospitalization with COVID-19 infection **(22).** This is in agreement with our results.

While cardiac troponins during the acute COVID-19 infection indicate myocardial inflammation and acute myocardial injury, LVGLS represents the clinical transformation of this myocardial injury into subclinical LV dysfunction **(23)**.

The reduction in LVGLS and elevation of cardiac troponin among COVID-19 patients may be due to various factors including viral infiltration of the myocardium that can lead to cardiomyocyte inflammation and death, respiratory failure and hypoxia that may cause myocardial injury, the immune response's activation and the release of cytokine storm that will cause myocardial inflammation and finally, microvascular dysfunction, coronary plaque thrombosis and rupture due to hypercoagulable state can also cause myocardial injury and inflammation **(24)**.

Conclusion:

Serial measurements of cardiac troponin and LVGLS following recovery from COVID-19 infection has an incremental

prognostic value and can be the ideal way to evaluate the progression of sub-clinical LV dysfunction.

Study limitations:

*Larger sample size and longer follow up period are needed to confirm the results.
*Further trials are needed to compare LVGLS and cardiac biomarkers with other inflammatory markers.

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