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SUBCLINICAL LEFT VENTRICULAR DYSFUNCTION IN PATIENTS RECOVERED FROM COVID-19 USING SPECKLE TRACKING ECHOCARDIOGRAPHY (STE) IN A TERTIARY CARE CENTRE IN INDIA

ANJOS P THANKACHAN [1], JAYARAM V. [2], D VINAYKUMAR [3]

[1] Senior Resident, Department Of Cardiology, Government T D Medical College and Hospital, NH-66, Vandanam Alappuzha, Kerala, India - 688005
+91-9496635894
tanjos007@gmail.com

[2] Associate Professor, Department Of Cardiology, Government T D Medical College and Hospital, NH-66, Vandanam Alappuzha, Kerala, India - 688005
+91-9847052586
drjram1966@gmail.com

[3] HOD & Professor, Department Of Cardiology, Government T D Medical College and Hospital, NH-66, Vandanam Alappuzha, Kerala, India - 688005
+91-9847015011
vinaykumard@gmail.com

ABSTRACT

Objectives:

To determine Subclinical left ventricular dysfunction in patients recovered from COVID-19 using speckle tracking echocardiography (STE) by Left Ventricular Global Longitudinal Strain Score (LVGLS).

Materials and Methods:

225 patients who visit post covid 19 clinic in Govt. medical college Alappuzha who satisfy the inclusion criteria selected. Speckle tracking ECHO was done to determine subclinical left ventricular dysfunction .by LVGLS score.

Results:

In the study, 25% of subjects had abnormal LVGLS The significant risk factors for reduced GLS are advancing age, diabetes ,clinical severity of Covid ,elevated inflammatory markers during active Covid.

Conclusions:

Subclinical left ventricular dysfunction was present in a quarter of patients who recovered from Covid 19.Elevated inflammatory markers during active Covid 19 is a predictor of subclinical left ventricular dysfunction during recovery.

Keywords: Covid recovery; Global longitudinal strain; Speckle tracking, LVGLS, Subclinical left ventricular dysfunction.

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1. INTRODUCTION

The COVID-19 pandemic has had a significant impact on global health, with millions of individuals infected and a devastating number of deaths worldwide.

During the acute phase of the infection, COVID-19 primarily affects the respiratory system, with symptoms such as cough, fever, and shortness of breath being the most commonly reported. However, emerging evidence suggests that COVID-19 can also have significant implications for cardiovascular health[1][2]. Most importantly, there has been a small but clinically relevant incidence of post-COVID-19 myocardial involvement in highly trained athletes, including myocarditis (1.1%), even in the presence of normal resting left ventricular function[3].

This phenomenon raises concerns about the potential long-term cardiovascular consequences of COVID-19, particularly in individuals who have recovered from the infection. COVID-19 in addition to acute complications, is also said to have long-term cardiovascular sequelae because of the cardiac injury caused by the novel coronavirus.

One of the key areas of concern is the development of subclinical left ventricular dysfunction in patients who have recovered from COVID-19. Studies have shown that cardiac involvement is present in a significant portion of patients recently recovered from COVID-19, independent of preexisting conditions or severity of the acute infection[4].Recent studies have reported subclinical left ventricular strain in approximately 30% of COVID-19 recovered individuals[5].Cardiac MRI imaging techniques have further confirmed the presence of myocardial inflammation and fibrosis in some recovered COVID-19 patients, indicating potential long-term cardiac damage and dysfunction

.Though cardiac MRI is the gold standard to detect subclinical left ventricular dysfunction, it is not feasible to perform this test on a large scale due to its cost and availability. Therefore, there is a need for non-invasive and cost-effective methods to assess subclinical left ventricular dysfunction in COVID-19 recovered individuals. One promising approach is the use of speckle tracking echocardiography, which allows for the assessment of myocardial deformation and strain.

2. MATERIALS AND METHODS

Study design and population

This was a descriptive study conducted in a tertiary care centre in India between October 2021 and October 2022. The study was approved by institution ethical committee and written informed consent was obtained from all participants before enrolment.

Patients who visit post covid 19 clinic in Government Medical College, Alappuzha who satisfy the inclusion criteria and are willing to participate in the study were included.

Inclusion criteria were those patients who have been recovered from Covid 19 Infection within the past 90 days. Exclusion criteria included patients having LV dysfunction in baseline trans thoracic ECHO (EF<50%),known coronary artery disease ,heart failure ,atrial fibrillation, ,previous cerebrovascular disease, renal failure (eGFR<30),poor echo window, age below 18yrs and above 80 years , patients who belonged to critically ill category of Covid 19 WHO Clinical severity classification .

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Data collection and Methodology

A detailed medical history, clinical examination, demographic data and of any associated illnesses are collected with the help of a structured questionnaire. Patients were categorised based on symptomatology and clinical features based on Living guidance for clinical management of COVID-19: World Health Organization (WHO) into mild ,moderate and severe disease after checking the discharge documents[6] .The level of inflammatory markers such as C-reactive protein (CRP), serum ferritin, and D-dimer during admission for covid was noted.

Speckle tracking ECHO

A Trans thoracic ECHO (VIVID GE echo machine) was performed and all baseline echocardiographic parameters such as left ventricular Ejection fraction (Teicholz method), LV diastolic function and right ventricular function (TAPSE) was recorded as per the American Society of Echocardiography (ASE) guidelines[7-9] .LVGLS was determined using two dimensional-STE. Three standard apical views (apical two chamber (A2C), apical three chamber (A3C), apical four chamber (A4C) views) were obtained at rest and for each of these views; well-defined cardiac cycles will be acquired and stored for offline analysis. The mean GLS will be calculated by averaging the peak GLS values of the three apical views.

A 17-segment polar plot (Bulls' eye) provided visual and quantitative representations of regional LV functions by plotting color-coded values of peak-systolic strain. A LVGLS value of < - 18 was considered abnormal [10].

Statistical Analysis

The sample size was calculated as 225 by using proportion of patients with LV dysfunction (p) from previous study, the reference study by Sudhanshu Mahajan[11] etal at GB Pant Hospital Delhi [(6).] Confidence level (1-a) of 95% and relative precision (d) as 20% of p

P=40/134=29.9

100-P=70.1

d=20% of p=5.98

$n= Z^2_{(1- a)} p(1-p)/d^2$

$z_{(1- a/2)}=1.96$

n=225

The sample size was calculated as 225

The data was entered in Microsoft excel and further statistical analysis was done Statistical package for Social Sciences (SPSS) software version 23. Continuous data was expressed as mean ± standard deviation (SD) and categorical data was represented as proportions. Comparison of means of continuous variables was done using Student's t-test. Correlation between inflammatory markers and LVGLS was done using Spearman correlation coefficient test. Multivariate logistic regression analysis was done to determine factors independently associated with reduced GLS. A two-sided P value of < 0.05 was considered to be statistically significant.

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3. RESULTS

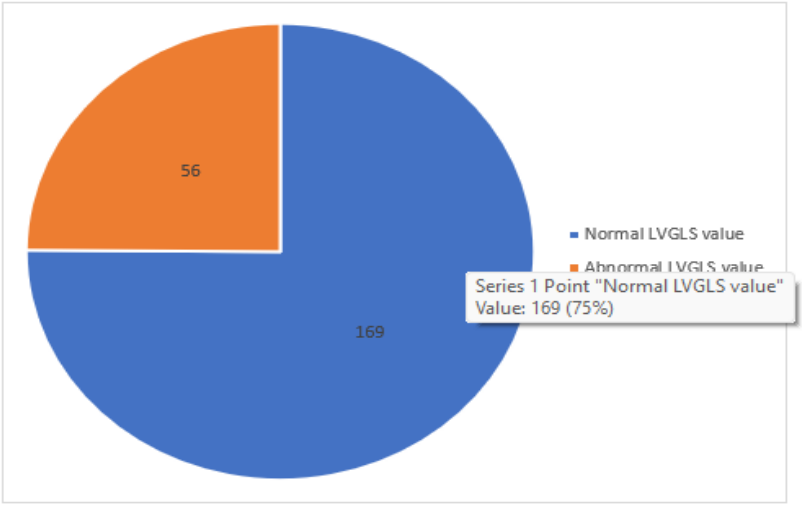
Baseline characteristics of study population

Patient Characteristics	Total(n=225)
Age(mean+/-SD)(years)	52.19+/-14.324
Gender	
Male	120(53.3%)
Female	105(46.7%)
WHO Clinical Category of Covid	
Mild	79(35.4%)
Moderate	57(25%)
Severe	89(39.6%)
Comorbidities	
Diabetes	85(37.8%)
Hypertension	123(54.7%)
COPD/Bronchial Asthma	90(40%)
Personal History	
Smoking	88(39%)
Alcohol	57(25%)
Predominant Post covid symptom	
Dyspnea	157(69.8%)
Chestpain	87(38.7%)
Palpitation	41(6.2%)
Syncope	3(1.3%)
Pedal Edema	14(6.2%)

Table 1. Baseline characteristics of study population

The mean age of the study sample is 52+/-14.324 with male predominance. Hypertension was the most prevalent comorbidity and the most common post covid symptom was dyspnea.

Distribution of study population according to LVGLS score



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Blue colour-Normal LVGLS (n=169) (75%)
Orange colour-Abnormal LVGLS (n=56) (25%)
Figure 1: Distribution of study participants according to their LVGLS score (n=225)

Figure 1 shows that of the 225 subjects studied,56 (25%) had abnormal LVGLS score. Figure shows that of the 56 subjects who had abnormal LVGLS 28(50%) were males and 28 were females (50%).The mean LVGLS score was 19.424+/-2.0804 with minimum of 15.4 and maximum of 22.5.

Abnormal LVGLS and age

Age group (in years)	31-40	41-50	51-60	61-70	71-80
Number of study participants with abnormal LVGLS score (percentage)	3(5.4%)	12(21.4%)	18(32.1%)	17(30.4%)	6(10.7%)

Table 2: Distribution of study participants with abnormal LVGLS score according to their age (n=56)

Of the 56 patients with abnormal LVGLS, 3(5.4%) are between the ages of 31 to 40 years, 12 (21.4%) between the ages of 41 to 50 years, 18 (32.1%) are between the ages of 51 to 60 years, 17 (30.4%) between the ages of 61 to 70 years and 6 (10.7%) are between the ages of 71 to 80 years. There is a statistically significant association ($p<0.05$) between abnormal LVGLS score and the age of the study participants.

Abnormal LVGLS and clinical category of Covid

WHO Category of Covid	**Number of subjects with abnormal LVGLS score(n=56)**
Mild	6 (10.7%)
Moderate	13 (23.2%)
Severe	37 (66.1%)

Table 3: Distribution of study participants with abnormal LVGLS score according to WHO Clinical Severity (n=56)

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Table 3 shows the distribution of study participants with abnormal LVGLS score according to the clinical category of covid. Of the 56 subjects with abnormal LVGLS, 6 (10.7%) were diagnosed with mild Covid-19, 13 (23.2%) with moderate disease and 37 (66.1%) with severe.There is a statistically significant association ($p<0.05$) between abnormal LVGLS and clinical category to which the patient belongs.

Abnormal LVGLS and inflammatory markers

	Mean	Standard deviation
Serum Ferritin Level (ng/mL)	253.787	215.2511
D-Dimer (ng/mL)	335.507	255.2212
hs-CRP (mg/L)	3.12	2.177

Table 4: Inflammatory markers in study population

Table shows the level of inflammatory markers in study subjects. There is moderate degree of negative correlation between LVGLS and Serum ferritin ($r=-0.493$, $p< 0.01$) and D-dimer ($r=-0.377$, $p< 0.01$). There is high degree of negative correlation between LVGLS and hs-CRP ($r=-0.511$, $p< 0.01$). This means that as the value of LVGLS decreases, the levels of inflammatory markers serum ferritin, D-dimer and hs-CRP increases.

Abnormal LVGLS and comorbidities

Comorbidities/Risk factors	Number of subjects with abnormal LVGLS(n=56)
Diabetes	41(73.2%)
Hypertension	31(55.4%)

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COPD/Bronchial Asthma	26(44%)
Alcohol Intake	16(28.6%)
Smoking	19(33.9%)

Table 5: Distribution of comorbidities and risk factors in patients with abnormal LVGLS (n=56)

Table 5 shows the presence of comorbidities in patients with abnormal LVGLS. There was statistically significant association between presence of diabetes and abnormal LVGLS ($p<0.05$).

Multivariable analysis for abnormal LVGLS

Logistic regression was performed to find out the significant factors associated with reduced GLS. The following factors were found to be significant risk factors for reduced GLS: hs-CRP, serum ferritin, D-dimer, age, diabetes, clinical severity of Covid-19 infection. The Cox and snell R square was found to be 0.378.

4. DISCUSSION

The findings of this study highlight the presence of subclinical left ventricular dysfunction in individuals who have recovered from COVID-19.This study adds to the growing body of evidence suggesting that COVID-19 can have long-term effects on cardiac health. Specifically, the study found that nearly 25% of participants had abnormal left ventricular global longitudinal strain, indicating subclinical left ventricular dysfunction. These findings are consistent with previous studies that have reported cardiac abnormalities in individuals who have recovered from COVID-19[12-15]. The Indian study conducted by Mahajan etal at Delhi showed results similar to our study with subclinical left ventricular dysfunction in 29 % of study subjects[11].

The suggested mechanisms include hypoxic injury to the heart, .ischemic injury caused by cardiac microvascular dysfunction including endotheliitis and vasculitis involving small cardiac vessels , formation of microthrombi, epicardial coronary artery disease with plaque destabilization and rupture or demand ischemia, stress cardiomyopathy or takotsubo cardiomyopathy, myocarditis, cytokine storm[16-18].

The study also found a significant association between the age of the participants and abnormal left ventricular global longitudinal strain, indicating that older individuals may be more susceptible to cardiac dysfunction following COVID-19 infection[19]. Moreover, the study found a significant association between the severity of COVID-19 infection and abnormal left ventricular global longitudinal strain. These findings suggest that older individuals with more severe cases of COVID-19 may be at a higher risk for developing cardiac complications.

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Furthermore ,comorbidities like diabetes was found to be associated with abnormal LVGLS .Diabetes is known to predispose individuals to cardiovascular complications due to detrimental effects on heart and blood vessels. Hyperglycemia, insulin resistance and chronic inflammation associated with diabetes can lead to cardiac remodelling and dysfunction. The combination of diabetes and Covid 19 may exacerbate this process leading to higher prevalence of subclinical left ventricular dysfunction

In addition to clinical variables, our study identified several biomarkers during active Covid 19 infection as potential risk factors for subclinical left ventricular dysfunction like elevated serum ferritin, D-Dimer and hs-crp. These biomarkers may reflect ongoing endothelial dysfunction, microvascular injury, myocardial inflammation and hypercoagulability.

These results have important clinical implications. They highlight the need for long-term cardiac monitoring and follow-up in individuals who have recovered from COVID-19, particularly in older individuals, those with more severe cases of the disease, comorbidities like diabetes and higher inflammatory markers during active Covid 19. This study emphasizes the importance of assessing left ventricular global longitudinal strain as a sensitive marker for detecting subclinical myocardial involvement in individuals who have recovered from COVID-19.Regular follow up with comprehensive cardiac evaluation including ECHO with LVGLS assessment may help detect and manage subclinical left ventricular dysfunction at an early stage.

5. CONCLUSION

Our study findings demonstrate a significant prevalence of abnormal LVGLS in patients recovered from Covid 19. Advancing age, clinical severity of Covid 19,diabetes, elevated hs-crp, D-dimer ,serum ferritin are identified as risk factors for subclinical left ventricular dysfunction .These findings emphasise the need for closer surveillance and timely interventions to mitigate long term cardiovascular risk in these vulnerable population.. Future research should elucidate the mechanism by which these risk factors contribute to subclinical left ventricular dysfunction and explore targeted interventions to optimise cardiovascular outcomes in patients recovered from Covid 19.

TABLES AND FIGURES CAPTIONS

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Table 4	Inflammatory markers in study population.
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REFERENCES

1. G. Sarra et al.. "Implications in oral health care for recovered cardiac patients: Long- term effects of COVID- 19 pandemic". Nov. 2020.
2. R. Rolfe, C. M. Smith and C. R. Wolfe. "The Emerging Chronic Sequelae of COVID-19 and Implications for North Carolina". Jan. 2021.
3. M. Vinciguerra, S. Romiti, G. Sangiorgi, D. Ritchie, F. Miraldi and E. Greco. "SARS-CoV-2 and Atherosclerosis: Should COVID-19 Be Recognized as a New Predisposing Cardiovascular Risk Factor?". Oct. 2021.
4. J. J. Bürgi et al.. "Mild COVID-19 induces early, quantifiable, persistent troponin I elevations in elder men". Dec. 2022.
5. H. Z. Wodschow et al.. "Oral ketone esters acutely improve myocardial contractility in post-hospitalized COVID-19 patients: A randomized placebo-controlled double-blind crossover study". Feb. 2023.
6. Living guidance for clinical management of COVID-19: Living guidance, 23 November 2021 – World Health Organization (WHO) : WHO/2019-nCoV/clinical/2021.2
7. . Potter E, Marwick TH. Assessment of left ventricular function by echocardiography: The case for routinely adding Global Longitudinal Strain to ejection fraction. J Am Coll Cardiol Img. 2018; 11: 260-74.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

8. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28: 1-39.
9. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2016; 29: 277-314.
10. Feigenbaum H., Mastouri R., Sawada S. A practical approach to using strain echocardiography to evaluate the left ventricle. *Circ J.* 2012;76:1550–1555
11. . Sudhanshu Mahajan, Shekhar Kunal, Bhushan Shah, et al. Subclinical left ventricular dysfunction in COVID-19 recovered patients using speckle tracking echocardiography. *Authorea.* June 01, 2021.
12. "Long-term cardiovascular outcomes in COVID-19 survivors .", thelancet.com.
13. "Prevalence and prognostic associations of cardiac abnormalities among post covid patients.", nature.com.
14. "Heart Problems after COVID-19,Johns Hopkins Medicine", hopkinsmedicine.org,
15. "Long-term cardiovascular outcomes of COVID-19 | Nature Medicine", nature.com
16. . Fox SE, Lameira FS, Rinker EB, Vander Heide RS. Cardiac Endotheliitis and Multisystem Inflammatory Syndrome After COVID-19. Ann Intern Med. 2020 Jul 29;L20-0882.
17. Giustino G, Croft LB, Oates CP, Rahman K, Lerakis S, Reddy VY, et al. Takotsubo Cardiomyopathy in COVID-19. J Am Coll Cardiol. 2020 Aug 4;76(5):628–9.
18. Daniels CJ, Rajpal S, Greenshields JT, Rosenthal GL, Chung EH, Terrin M, et al. Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection. JAMA Cardiol. 2021 Sep;6(9):1078–87. 70