2-D speckle tracking echocardiographic evaluation of mild post-COVID patients

Hülya Çelik[1], Betul Cengiz[1], Şükrü Şahin[1], Vedat Aytekin[2], and Saide Aytekin[2]

[1]American Hospital
[2]Koç University School of Medicine

March 13, 2023

Abstract

Objectives: COVID-19 has been the primary health problem and because of the virus affinity to endothelial cells, it has become an important reason of vascular problems and cardiac injury. After mild COVID-19 infection, patients frequently attend to the cardiology clinics with cardiac symptoms and their primary cardiac tests are mostly normal. The aim of the study is analysing if the difference of cardiac deterioration could be shown with 2D-speckle tracking echocardiography between symptomatic and asymptomatic patients when transthoracic echocardiography parameters are normal. **Methods:** In this retrospective single centre study, total of 2741 transthoracic echocardiography records were assessed and post-COVID patients (n:108) were detected and divided into 'symptomatic' and asymptomatic' patient groups and left ventricular global longitudinal strain values were compared. **Results:** The number of patients with normal global longitudinal strain values were equal in the groups and the number of patients with impaired GLS values in the symptomatic group were more than the asymptomatic group (15 patients in the symptomatic group and 4 patients in the asymptomatic group) and the difference was statistically different (p=0,008). The average GLS values were -18,88±2,50 in the asymptomatic group and -17,40±3,68 in symptomatic group but the difference was not statistically significant (p=0,098) **Conclusion:** More symptomatic patients than the asymptomatic ones have impaired left ventricular GLS values according to the results of this study. Even if it is not statistically significant, the mean left ventricular GLS values are also reduced in symptomatic patients after mild COVID-19 infection.

2-D speckle tracking echocardiographic evaluation of mild post-COVID patients

Hülya Gamze Çelik[a] MD, Betül Cengiz Elçioğlu[a] MD, Şükrü Taylan Şahin[a]MD, Vedat Aytekin[b] MD, Saide Aytekin[b] MD

[a] Department of Cardiology, American Hospital, Istanbul, Turkey

[b] Department of Cardiology, Koç University School of Medicine, Istanbul, Turkey

Correspondence

Hülya Gamze Çelik, Department of Cardiology, American Hospital, Istanbul, Turkey

E-mail: gguremek@yahoo.com

Abstract

Objectives: In recent years, COVID-19 has been the primary health problem and because of the virus affinity to endothelial cells, it has become an important reason of vascular problems and cardiac injury. After mild COVID-19 infection, patients frequently attend to the cardiology clinics with cardiac symptoms like chest pain, shortness of breath, palpitations, and reduced exercise capacity and their primary cardiac tests are mostly normal. The aim of the study is analysing if the difference of cardiac deterioration could be shown with 2D-speckle tracking echocardiography between symptomatic and asymptomatic post-COVID patients when transthoracic echocardiography parameters are normal.

Methods: In this retrospective single centre study, total of 2741 transthoracic echocardiography records were assessed and post-COVID patients (n:108) were detected and divided into 'symptomatic' and asymptomatic' patient groups and left ventricular global longitudinal strain values were compared.

Results: The number of patients with normal global longitudinal strain (GLS) values were equal in the groups and there were 4 patients whose GLS values were borderline in the asymptomatic group, while there was none in the symptomatic group. The number of patients with impaired GLS values in the symptomatic group were higher than the asymptomatic group (15 patients in the symptomatic group and 4 patients in the asymptomatic group) and the difference was statistically different (p=0,008). The average GLS values were -18,88±2,50 in the asymptomatic group and -17,40±3,68 in symptomatic group but the difference was not statistically significant (p=0,098)

Conclusion: More symptomatic patients than the asymptomatic ones have impaired left ventricular GLS values according to the results of this study. Even if it is not statistically significant, the mean left ventricular GLS values are also reduced in symptomatic patients after mild COVID-19 infection.

KEY WORDS

echocardiography, speckle tracking echocardiography, global longitudinal strain, post-COVID

Introduction

In recent years, COVID-19 has been the primary health problem and because of the virus affinity to endothelial cells, it has become an important reason of vascular problems and cardiac injury. Acute pericarditis, acute myocarditis and myocardial infarction are the main clinical manifestations especially among patients treated in the intensive care unit (1-4). Even though the potential pathogenesis of the cardiac injury is not clear, the direct effect to ACE2 receptor and hyperimmune response during sitokin storm are highly suspected (5-7) and up to 7% of the COVID-related deaths have been attributed to myocarditis (8).

After mild COVID-19 infection, patients frequently attend to the cardiology clinics with cardiac symptoms like chest pain, shortness of breath, palpitations, and reduced exercise capacity and their primary cardiac tests are mostly normal. Because of the potential of possible myocardial injury of the disease, simply applicable advanced techniques like 2-D speckle tracking echocardiography (2D-STE), would be a better method than conventional transthoracic echocardiography (TTE) for evaluating regional and global myocardial deformation because it's independent of angle and can diagnose subclinical myocardial dysfunction earlier (11-14).

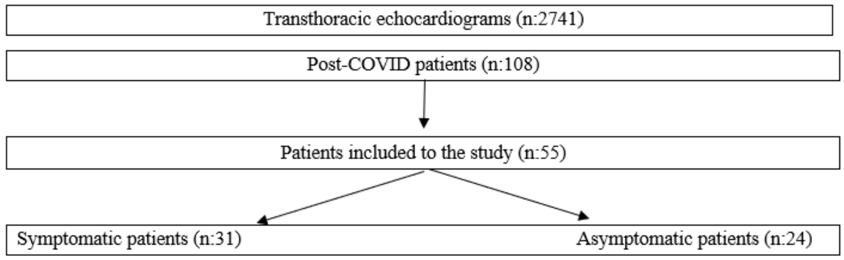
The aim of the study is analysing if the difference of cardiac deterioration could be shown with 2D-STE between symptomatic and asymptomatic post-COVID patients when TTE parameters are normal.

Materials and Methods

In this retrospective single centre study, total of 2741 TTE records in American Hospital's Echocardiography laboratory between January 2021-August 2021 were assessed. Post-COVID patients (n:108) were detected. The inclusion criteria of involvement to the study are having had COVID-19 diagnosis by polymerase chain reaction (PCR) test positiveness in the last 6 months and to be older than 18 years old. Exclusion criteria were designated as; to be hospitalized because of moderate or severe COVID-19 infection, having passed more than 6 months after COVID-19 infection, severe valvular heart disease, segmental/global left ventricular systolic disfunction, known coronary artery disease, conduction disorder, rhythms other than normal sinus rhythm and not having enough imaging frames of echocardiography for calculating LV-GLS. After the exclusion criteria, 31 patients were detected for 'symptomatic group' throughout total included 55 patients. (Figure 1).

The study protocol was approved by the Local Ethics Committee as a retrospective single centre study and was conducted according to the Declaration of Helsinki.

Figure 1: Study protocol



Transthoracic Echocardiography

TTE was performed at the day the patient presented to the cardiology clinic with Phillips EPIC CVx, Phillips Healthcare, Inc., Andover, MA, USA X5-1 matrix transducer. Left ventricular end-diastolic (LVD) and end-systolic (LVS) diameters, left ventricular posterior wall thickness (PW) and interventricular septum thickness (IVS) were measured from parasternal long axis view. Left atrium (LA), right atrium (RA) and right ventricular end-diastolic basal diameters (RV) were measured from the apical four-chamber view. Left ventricular ejection fraction (LVEF) was calculated with modified Simpson's method from the apical four chamber view (15,16). The systolic pulmonary artery pressure (sPAP) was calculated from the sum of tricuspid regurgitation peak velocity and estimated RA pressure (16).

Speckle Tracking Echocardiography

LV apical 4-chamber, 2-chamber, and 3-chamber views which were stored during TTE in a frame rate of 60 to 100 frames per second (17) for images of 3 consecutive cardiac cycles were used for offline analysis. Imaging analysis was performed on the Phillips EPIC CVx's QLAB software. The LV endocardial border of the end-systolic frame was automatically traced by the program and manually corrected if necessary. The software automatically created a region of interest including the entire transmural wall for all the patients and selected natural acoustic markers moving with the tissue. Automatic frame by-frame tracking of these markers during the cardiac cycle (2-dimensional [2D] systolic time interval method) yielded a measure of strain, and strain rate at any point of the myocardium. Left ventricular global longitudinal strain (LV-GLS) were measured by averaging the values of all segments.

The standard normal LV-GLS limit was defined as >-18% (18). The impaired GLS level was accepted as <-16%. The measurements between these levels were accepted as borderline (-18%) – (-16%) (19).

Statistical Analysis

The statistical analysis was performed with SPSS version 26. Categorical variables were represented as percentages while the numerical variables were determined as arithmetic mean ± standard deviation. Wilcoxon test was used for comparison of the averages of the data and Ki-square test was used for the comparison of the percentages of the data between groups. The significance levels of 0,05 and 0,001 values were considered for the study.

Results

Total of 55 patients were in the study group and divided into symptomatic (n:31) and asymptomatic (n:24) groups. Only the average age of the patients between the groups was statistically different and there was not a statistically significant difference between the other demographic and clinic features of the groups. The number of female patients were 27 (%49,09) in the study group. (Table 1)

Table 1. The demographic and clinical features of the study groups

Parameter	Asymptomatic (n=24)	Symptomatic (n=31)	p value
Gender (Female) (%)	13(%54,2)	14(%45,2)	0,508
Age	52.25±14.98	44,38±11.98	0,036
BMI	25.79±2,35	25,4±3,18	0,617
SBP	124.33±9,95	124,48±13,54	0,964
DBP	79,08±6,15	80,35±9,32	0,566
Heart Rate (bpm)	70.3±11,15	74,8±11,8	0,063
Hypertension n (%)	6 (25)	5(16,7)	0,659
Diabetes Mellitus (%)	4(16,7)	1(3,3)	0,227
Hyperlipidemia (%)	3(12,5)	2(6,7)	0,722
ACE-I n (%)	0(0)	3(10)	0,267
ARB n (%)	6(25)	3(10)	0,303
Beta Blockers n (%)	3(12,5)	2(6,7)	0,722
Statin n (%)	2(8,3)	2(6,7)	0,935

SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; ACE-I: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker

The conventional echocardiographic parameters were similar and were not statistically different between two groups (Table 2).

Table 2. The echocardiographic measurements of the groups

Parameter	Asymptomatic (n=24)	Symptomatic (n=31)	p value
LV EF (%)	60 ± 3	60 ± 2	0,494
PAPs (mmHg)	25,5 ± 3,9	24,9±5,4	0,297
IVS (cm)	0,95±0,13	0,94±0,14	0,601
PW (cm)	0,88±0,11	0,90±0,13	0,790
LVEDD (cm)	4,60±0,37	4,61±0,38	0,821
LVESD (cm)	3,01±0,31	2,99±0,31	0,400
LA (cm)	3,41±0,26	3,42±0,34	0,120
RA (cm)	3,66±0,30	3,58±0,34	0,528
RV (cm)	3,31±0,39	3,31±0,38	0,678
E/A ratio	1,07±0,26	1,08±0,20	0,838

LV EF: left ventricular ejection fraction; PAPs: systolic pulmonary arterial pressure; IVS: interventricular septal thickness; PW: posterior wall thickness; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end systolic diameter; LA: left atrium; RA: right atrium; RV: right ventricle.

The number of patients with normal GLS values were equal in the groups and there were 4 patients whose GLS values were borderline in the asymptomatic group, while there was none in the symptomatic group. The number of patients with impaired GLS values in the symptomatic group were higher than the asymptomatic group (15 patients in the symptomatic group and 4 patients in the asymptomatic group) and the difference was statistically different (p=0,008). The average GLS values were -18,88±2,50 in the asymptomatic group and -17,40±3,68 in symptomatic group but the difference was not statistically significant (p=0,098). The distribution of the number of the patients according to the GLS borders is shown in Figure 2 and the distribution of patients in the impaired GLS values and the average GLS values of the groups are shown in

Table 3.

Figure 2. The GLS values in symptomatic and asymptomatic patients

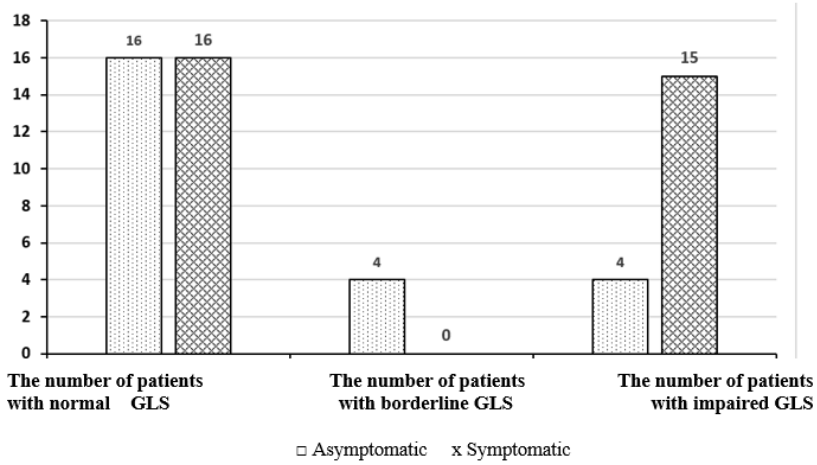


Table 3 . The distribution of patients with impaired GLS values

Parameter	Group	Asymptomatic	Symptomatic	p value
GLS values	*Impaired*	4 (n)	15 (n)	**0,008**
	Mean±S.D (%)	-18,88±2,50	-17,40±3,68	**0,098**

Discussion

TTE is the main imaging technique to investigate LV structure and functions, but conventional echocardiographic techniques may not be enough to show the pre-clinic mechanical deterioration. 2D-STE is a better method for evaluating regional and global myocardial deformation and can diagnose subclinical myocardial dysfunction earlier and may detect patients who needs further investigations, cardiac controls, and myocardial protection (11-14).

In our study we evaluated the difference of left ventricular myocardial functions with LV-GLS between asymptomatic and symptomatic patients who had mild COVID infection. Życzkowska et al also investigated mild COVID infection's effects in heart functions including standard and advanced echocardiographic techniques but the result of the study did not show significant impairment in left ventricle functions (20).

The real prevalence of the cardiac involvement is not clear, and the study results are conflicting. It can be speculated that these results may be related with the study populations. In a study from a single tertiary centre, Erdol et al evaluated 100 consecutive COVID-19 proven patients after quarantine period with CMR and cardiac involvement was detected in 49 patients in which 41 patients described cardiac symptoms that were not present before COVID infection, and the results were statistically significant (p=0,001). In 24 patients out of 51 who does not have cardiac involvement in CMR were asymptomatic and this result was also statistically significant (p=0,001) (21).

As it's known that the 2D-STE and CMR results are compatible with each other, 2D-STE for LV quantification has been validated against MRI (22). Puntmann at al. evaluated left ventricle with CMR after mild COVID infection without known cardiac disease and showed more diffuse myocardial edema at follow-up in patients with ongoing symptoms as compared to the ones who has improved. They also investigated the LV-GLS values between the control and post-COVID patients and even though the average values of LV-GLS were in normal ranges in both groups, the difference was statistically different (23). In our study, even the average LV-GLS value was lower in the symptomatic group, the difference was not statistically different.

In another hybrid study using both TTE, 2D-STE and CMR, Brito et al. evaluated young athletes who had mild to moderate degree COVID-19 infection. Even no athlete showed ongoing myocarditis imaging features, the result of this study shows that mild or asymptomatic COVID-19 is not a benign illness, as more than one-half of the younger individuals showed subclinical myocardial and pericardial disease (24). The reduction of LV-GLS values is seemed to be obtained mostly in symptomatic patients or in patients who have an additional finding as pericardial involvement, and it is independent of the COVID-19 disease severity.

The limitations of our study are, it's a single centre retrospective study and the GLS values of our study population are not known before the COVID infection, and the number of the study population is low because we have stopped including patients after August 2021, the date that the m-RNA vaccines are applied to the general population in Turkey to avoid the effects of m-RNA vaccine's myocardial damage and myocarditis side effect.

Conclusion

Despite the small number of the patients in the study group, the results of this study show that more symptomatic patients than the asymptomatic ones have impaired LV-GLS values. Even if it is not statistically significant, the mean LV-GLS values are also reduced in symptomatic patients after mild COVID-19 infection. It can be concluded that close follow-up of these patients in the future may be beneficial until randomized controlled studies with high numbers of patients are conducted.

Acknowledgment

None

Funding

This submission is not supported by external funding.

Disclosures

The authors have no relevant financial or non-financial conflicts of interest to disclose.

ORCID: Hülya Gamze Çelik MD: https://orcid.org/0000-0001-6883-3197

Betül Cengiz Elçioğlu MD: *https://orcid.org/0000-0002-9310-3767*

Şükrü Taylan Şahin MD: *https://orcid.org/0000-0003-4080-3919*

Vedat Aytekin MD: *https://orcid.org/0000-0003-2761-7572*

Saide Aytekin MD: *https://orcid.org/000-0003-1968-0889*

References

1.Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395:497-506.

2.Badano LP, Kolias TJ, Muraru D, et al. Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/industry task force to standardize deformation imaging. Eur Heart J Cardiovascc Imaging.2018;19(6):591-600.

3.Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet.2020;395(10229):1054-1062.

4.Mitrani RD, Dabas N, Goldberger JJ. COVID-19 cardiac injury: implications for long term surveillance and outcomes in survivors. Heart Rhythm.2020;26:1-7.

5.Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RD. Features, evaluation, and treatment coronavirus (COVID-19), in StatPearls [internet]. Treasure Island: StatPearls; 2020. https://www.ncbi.nlm.nih.gov/books/NBK554776/. Accessed 10 Aug 2020.

6.Orrico J. Coronavirus and heart. 2020. https://news.harvard.edu/ gazette/story/2020/04/covid-19s-consequences-for-the-heart/. Accessed 14 Apr 2020.

7.Behrens EM, Koretzky GA. Review: cytokine storm syndrome: looking toward the precision medicine era. Arthritis Rheumatol. 2017;69(6):1135–43.

8.Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol. 2020; 75:2352-2371.

9.Bonow RO, Fonarow GC, O'Gara PT, Yancy CW. Association of coronavirus disease 2019 (COVID-19) with myocardial injury and mortality. JAMA Cardiol. 2020.

10.Xiong TY, Redwood S, Prendergast B, Chen M. Coronaviruses and the cardiovascular system: acute and long-term implications. Eur Heart J. 2020;41(19):1798–1800.

11.Blessberger H, Binder T (2010) Non-invasive imaging: Two dimensional speckle tracking echocardiography: basic principles. Heart 96:716–722

12.Kalam K, Otahal P, Marwick TH (2014) Prognostic implications of global LV dysfunction: a systematic review and metaanalysis of global longitudinal strain and ejection fraction. Heart 100:1673–1680

13.Carluccio E, Biagioli P, Alunni G et al (2018) Prognostic value of right ventricular dysfunction in heart failure with reduced ejection fraction: superiority of longitudinal strain over tricuspid annular plane systolic excursion. Circ Cardiovasc Imaging 11:e006894

14.Xie M, Li Y, Cheng TO et al (2015) The efect of right ventricular myocardial remodeling on ventricular function as assessed by two-dimensional speckle tracking echocardiography in patients with tetralogy of Fallot: a single center experience from China. Int J Cardiol 178:300

15.Schiller NB, Acquatella H, Ports TA et al (1979) Left ventricular volume from paired biplane two-dimensional echocardiography. Circulation 60(3):547–555

16.Feigenbaum H, Armstrong WF, Ayan T. Feigenbaum's Echocardiography. 6th ed. Lippincott's Williams&Wilkins; 2005. p. 355–6.

17. Mizuguchi Y, Oishi Y, Miyoshi H, Iuchi A, Nagase N, Oki T. The functional role of longitudinal, circumferential, and radial myocardial deformation for regulating the early impairment of left ventricular contraction and relaxation in patients with cardiovascular risk factors: a study with two-dimensional strain imaging. J Am Soc Echocardiogr 2008; 21:1138–44

18.Marwick TH, Leano RL, Brown J et al (2009) Myocardial strain measurement with 2-dimensional speckle-tracking echocardiography: definition of normal range. JACC Cardiovasc Imaging 2:80–84

19. Lang RM, Badano LP, Mor-Avi V et al (2015) Recommendations for cardiac chamber quantifcation by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 28:1–39

20. Uzię bło-Życzkowska B, Krzesinski P, Domino B, Chcialowski A, Maciorowska M, Gielerak G (2021) Echocardiographic assessment of cardiac function after mild coronavirus disease 2019: A preliminary report. J Clin Ultrasound. 2022 Jan;50(1):17-24. Doi: 10.1002/jcu.23094.

21. Erdol MA, Ozbay MB, Yayla C, Arslan H, Ozbulbul NI, Cetin EHO, Karanfil M, Erdogan M, Demirtas K, Ertem AG, Akcay AB (2021) Cardiac involvement in MRI in young population after COVID-19: A single tertiary center experience. 2021 Aug;38(8):1327-1335. Doi: 10.1111/echo.15160. Epub 2021 Jul 19

22. Amundsen B.H., Helle-Valle T., Edvardsen T., *et al.*Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. J Am Coll Cardiol, 47 (2006), pp. 789-793)

23. Puntmann V.O., Martin S, Shchendrygina A, Hoffmann J, Ka M.M. et al. Long-term cardiac pathology in individuals with mild initial COVID-19 illness. Nat Med, 2022. PMID: 36064600. doi: 10.1038/s41591-022-02000-0

24. Brito D, Meester S, Yanamala N, Patel HB, Balcik BJ, Casaclang-Verzosa G, Seetharam K, Riveros D, Beto 2nd RJ, Balla S, Monseau AJ, Sengupta PP. (2020) High Prevalence of Pericardial Involvement in College Student Athletes Recovering From COVID-19. JACC Cardiovasc Imaging. 2021 Mar;14(3):541-555. Doi: 10.1016/j.jcmg.2020.10.023 Epub 2020 Nov 4