Research Brief

Post covid assessment of right and left ventricular global longitudinal strain

R. Rameshwar, K. Meenakshi*, Gowtham Hanumanram, R. Kannan, S. Magesh Kumar, J. Damodaran, S. Nandhini
Saveetha Medical College and Hospital, Chennai, Tamilnadu, India

1. Introduction

Cardiac dysfunction has been reported in SARS-CoV2 infection.1 Most studies of ventricular function in covid patients were during the acute infection and there are very few studies during post covid convalescence.2 Two Dimensional echocardiography(2D ECHO) is mandatory in all dyspnoeic post covid patients to look for persistent or new onset overt cardiac dysfunction as evidenced by reduced ejection fraction(EF) or a subtle cardiac dysfunction as determined by global longitudinal strain(GLS), even after they have turned covid negative. GLS has been proven to be a sensitive determinant of myocardial dysfunction and antedates the reduction of ejection fraction(EF).

2. Methods

Aim- To assess if subclinical myocardial dysfunction indicating a smouldering myocarditis, could be identified by GLS in post COVID19 patients who have become covid negative.

Study cohort – 100 patients.

Inclusion criteria - Covid 19 patients admitted with breathlessness.
Exclusion criteria - Patients with poor ECHO window.

All patients underwent at admission, routine 2D ECHO to detect ventricular dysfunction, Inflammatory markers like C reactive protein(CRP), serum Ferritin, D Dimer, Neutrophil lymphocyte ratio(NLR), serum albumin and CT chest, in addition to routine tests. Interleukin(IL)6 and troponin I were assayed when indicated.

Two weeks later, after they had become covid negative, they underwent another 2D ECHO along with determination of left ventricular(LV) and right ventricular(RV) GLS to detect subtle cardiac dysfunction.

ECHO was done with Vivid T8 Echo machine and 3.5 Mhz transducer. EF <50% was taken as overt LV systolic dysfunction. Tricuspid annular plane systolic excursion(TAPSE) < 15 mm was taken as overt RV dysfunction. The GLS was determined by speckle tracking and normal LVGLS was taken as /C0 18% and above and normal RV GLS as /C0 24% and above.

3. Results

Initial ECHO in these patients revealed overt LV systolic dysfunction in 4%, LV diastolic dysfunction in 57% and overt RV dysfunction in 2%. 2D ECHO, 2 weeks later revealed that 51% had reduced GLS viz; 18%, 21% and 12% had reduced LV GLS, reduced RV

* Corresponding author. Department of Cardiology, Saveetha Medical College, Thandalam, Chennai, India.
E-mail address: drmeenaram@gmail.com (K. Meenakshi).
GLS and reduced biventricular GLS respectively. 36% had pulmonary hypertension of varying severity. Table 1.

Table 1
Distribution of Overt & Covert LV & RV dysfunction.

|                  | REDUCED LV GLS (18%) | REDUCED RV GLS (21%) | REDUCED BIVENTRICULAR GLS (12%) |
|------------------|----------------------|----------------------|----------------------------------|
| NORMAL EF        | 18%                  | REDUCED EF           | 21%                              |
| 0                |                      | NORMAL TAPSE         | REDUCED TAPSE                    |
|                  | 8%                   |                      | 4%                               |
|                  |                      | NORMAL EF            | REDUCED EF                       |
|                  | 10%                  |                      | 2%                               |

Table 2
Relation of GLS to CRP levels.

| GLS                  | CRP 10 mg/L | CRP 11-50 mg/L | CRP 50-100 mg/L | CRP >100 mg/L |
|----------------------|-------------|----------------|----------------|--------------|
| LV & RV GLS (Normal) | 49          | 11(22.4%)      | 28(57.2%)      | 0            |
| LV GLS (Reduced)     | 18          | 1(5.6%)        | 3(16.7%)       | 2(11.1%)     |
| RV GLS (Reduced)     | 21          | 0              | 3(14.3%)       | 18(85.7%)    |
| LV & RV GLS (Reduced)| 12          | 0              | 1(8.3%)        | 11(91.7%)    |

Fig. 1. Relation between GLS & Interleukin 6 levels(IL6).

Table 3
Relation between D Dimer levels and GLS.

| GLS                  | D DIMER NORMAL | D DIMER 250-400 | D Dimer 400-2000 | D Dimer >2000 |
|----------------------|----------------|-----------------|------------------|---------------|
| LV & RV GLS (Normal) | 49             | 13(26.5%)       | 36(73.5%)        | 0             |
| LV GLS (Reduced)     | 18             | 1(5.6%)         | 2(11.1%)         | 1(5.6%)       |
| RV GLS (Reduced)     | 21             | 0               | 2(9.5%)          | 1(4.8%)       |
| RV & LV GLS (Reduced)| 12             | 0               | 1(8.3%)          | 10(83.4%)     |

Table 4
Relation between Serum ferritin & GLS.

| GLS                  | ferritin NORMAL | ferritin 251-500 | Ferritin >500 |
|----------------------|-----------------|------------------|--------------|
| LV & RV GLS (Normal)| 49              | 18(36.7%)        | 31(63.3%)    | 0            |
| LV GLS (Reduced)     | 18              | 2(11.1%)         | 2(11.1%)     | 14(77.8%)    |
| RV GLS (Reduced)     | 21              | 3(14.3%)         | 2(9.5%)      | 16(76.2%)    |
| RV & LV GLS (Reduced)| 12              |                  |              | 12(100%)     |

GLS and reduced biventricular GLS respectively. 36% had pulmonary hypertension of varying severity. Table 1.

The GLS was compared to the inflammatory marker levels. 81.4% with reduced GLS had CRP >100 mg/L. Table 2.

60% with normal LV & RV GLS had normal IL6, while 66.7% with reduced LVGLS, 90.5% with reduced RVGLS and 83.3% with reduced biventricular GLS had IL6 >25 pg/ml [Fig. 1].

Patients with normal RV & LV GLS had D Dimer <400 ng/ml 77.7% with reduced LVGLS, 85.7% with reduced RV GLS and 83.4% with reduced biventricular GLS had D Dimer >2000 ng/ml [Table 3].

36.7% with normal LV & RV GLS had normal serum ferritin, while 63.3% had serum ferritin between 250 and 400 ng/ml 77.8% with reduced LV GLS, 76.2% with reduced RV GLS and 100% with reduced biventricular GLS had serum ferritin >500 ng/ml [Table 4].
84.4% with reduced GLS had CT severity scores >15/25. **Fig. 2.**
The NLR was <3.5 in 30.6% and 3.5–5 in 65.3% with normal LV & RV GLS. 100% with reduced LV GLS, 66.7% with reduced RV GLS and 83.4% with reduced biventricular GLS had NLR >10 (Table 5).

51% with normal LV & RV GLS had normal serum albumin levels in contrast to 77.8%, 81% and 91.7% of patients with reduced LV GLS, Fig. 3. **Relationship between Global longitudinal strain (GLS) & Serum albumin levels.**

**Table 5**

| GLS                  | NLR <3.5 | NLR >3.5–5 | NLR 6–9 | NLR >10 |
|----------------------|----------|------------|---------|---------|
| LV GLS & RV GLS (Normal) 49 | 15 (30.6%) | 32 (65.4%) | 1 (2%)  | 1 (2%)  |
| LV GLS (Reduced) 18  | 0        | 0          | 0       | 18 (100%) |
| RV GLS (Reduced) 21  | 1 (4.7%) | 3 (14.3%)  | 3 (14.3%)| 14 (66.7%) |
| RV & LV GLS (Reduced) 12 | 0  | 1 (8.3%)  | 1 (8.3%) | 10 (83.4%) |

**Table 6**

| LV GLS & Duration between Symptom Onset and Admission |
|-----------------------------------------------------|
| <4 DAYS                                             |
| >4 DAYS                                             |
| LV GLS & RV GLS (Normal) 49                        |
| 49 (100%)                                           |
| 0                                                   |
| LV GLS (Reduced) 18                                 |
| 5 (27.8%)                                           |
| 13 (72.2%)                                          |
| RV GLS (Reduced) 21                                 |
| 11 (52.4%)                                          |
| 10 (47.6%)                                          |
| RV & LV GLS (Reduced) 12                            |
| 0                                                   |
| 12 (100%)                                           |
reduced RV GLS and reduced biventricular GLS respectively, who had serum albumin <2.9 g/dl (Fig. 3).

There were no comorbidities in 63.3% with normal LV & RV GLS, 61.1% with reduced LV GLS and 61.9% with reduced RV GLS. 100% with normal GLS were admitted within 5 days of symptoms onset in contrast to 73.3% with reduced GLS who were admitted 5 days after symptoms onset (Table 6).

77.6% with normal LV and RV GLS and 61.9% with reduced RV GLS were <50 yrs. 72.2% with reduced LV GLS and 66.7% with biventricular GLS were >50 yrs.

51.2% of males and 50% of females had reduced GLS.

4. Discussion

Subclinical LV dysfunction in ECHO has been observed in 30%–80% of COVID 19 patients. Our study shows that 51%, 2 weeks after diagnosis of covid had reduction of LV or RV or biventricular GLS.

Zhou et al reported higher troponin levels in covid non survivors. All our patients with ECG changes or EF <50% had elevated serum troponin I levels.

A retrospective study of COVID19 patients indicated that CRP is an independent predictor of severe infection. In our study, 81.3% with reduced GLS had CRP >100.

A meta-analysis of 9 studies reported mean IL-6 values 3 times higher in complicated Covid. IL-6 >25 pg/ml occurred in 80.1% with reduced GLS.

Significantly higher D-Dimer levels were reported as a prognostic marker in severe covid. 82.2% of our patients with reduced GLS had D Dimer >2000.

Literature reports elevated serum ferritin as an independent indicator of severe covid. In our study 85% with reduced GLS had serum Ferritin values > 500 pg/ml.

CT severity score semi quantitatively estimates lung involvement with a total score from 0 to 25. 84% with reduced GLS in our study had CT score >15/25.

Lymphopenia in COVID19 is an independent prognostic marker. NLR >10 was seen in 83.3% of our patients with reduced GLS.

Hypo albuminemia occurs in severe covid. 83% of our patients with reduced GLS had Serum albumin <2.9 g/dl.

Older age, male sex and co morbidities have been reported as risk factors for cardiac involvement in covid. We did not find any clear difference however.

Literature indicates higher morbidity in patients seeking medical help late. Most of our patients with reduced GLS had sought treatment 5 days or more after onset of symptoms.

The 12% with reduced biventricular GLS, had a stormy course with a 5–9 day ICU stay. Biventricular strain imaging has been sparsely studied in covid. One study in acute covid reported reduced biventricular strain as predictive of higher mortality.

5. Conclusion

Overt cardiac manifestations seen in covid 19 represent the tip of the iceberg. Incipient cardiac dysfunction, which could have long term cardiac repercussions are more prevalent than known and can be detected by assessment of GLS, even 2 weeks after admission and after the patient became covid negative. The GLS reduction post covid, mandates the need to seek medical help early, even before the reduction of the EF and to follow up adequately, to see if it improves, remains as such or progresses and to prevent acute episodes of overt cardiac dysfunction.

References

1. Pirzada Ashar, Mokhtar Ahmed T, Moeller Andrew D. COVID-19 and myocarditis: what do we know so far? QJ open. 2020;2:278–285.
2. Shnueli Hezzy, Shah Maulin, Ebinger Joseph E, Long-Co Nguyen, Fernando Chernomordik, et al Left ventricular global longitudinal strain in identifying subclinical myocardial dysfunction among patients hospitalized with COVID-19. J Card & Vasculature. 2021;32(1):100719.
3. Sadeghi-Haddad-Zavareh Mahmoud, Bayani Masoomeh, Shokri Mehran, Ebrahimpour Soheil, Babazadeh Arefeh, et al C-reactive protein as a prognostic indicator in COVID-19 patients. Hindawi Interdisciplinary Perspectives on Infections Diseases. 2021. Article ID 5557582.
4. Aiz M, Fatima R, Assaly R. Elevated interleukin-6 and Severe COVID-19: a meta analysis. J Med Virol. 2020.
5. Yao Yumeng, Cao Jiatian, Wang Qingqing, Shi Qinfeng, Liu Kai, et al D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. Journal of Intensive Care. 2020;8:49.
6. Bozkurt F, Tercan M, Patmano G, et al. (January 21, 2021) can ferritin levels predict the severity of illness in patients with COVID-19. Cureus 13(1): e12832.
7. Franco Marco, Franco Iafrate, Maria Masci Giorgio, Coco Simona. Francesco Cilia et al Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol. 2020 Jul 4;1–10.
8. Sy Chana Abigail, Amit Rout. Use of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in COVID-1. J Clin Med Res. July 2020;12:448–453. Number 7.
9. Jiaofeng Huang , Aiguo Cheng , Rahul Kumar , Yangqing Fang , Gongqing Chen: Hypoalbuminemia predicts the outcome of COVID-19 in patients of age and co-morbidity. J Med Virol2020 Oct;92(10):2152-2158.
10. Chang Wei-Ting, Han Siong Toh, Liao Chia-Te, Wen-Liang Yu. Cardiac involvement of covid-19: a comprehensive review. The American journal of the medical sciences;volume361, issue:January 01, 2021;1:p14–p22.
11. Ahmed Alaa, Qian Zhaozhi, Rashed Jem, Benger Jonathan, van der Schaar Mihaela. Retrospective cohort study of admission timing and mortality following COVID-19 infection in England. BMJ Open. 2020;10,e042712.
12. 1,2, Jie Yuji, Wang Lufang, Li Meng, Li He, Zhu Shuangshuang. Biventricular longitudinal strain predict mortality in COVID-19 patients, 1,2, J Front Cardiovasc Med. 2020;7:832434, 1,2,1,2.