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Left Atrial Strain evaluation in Post Covid 19 Recovered Patients

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ABSTRACT

Background: The COVID-19 pandemic has affected more than 170 million people around the world, and previous studies of complications and long-term effects of SARS-CoV-2 infection have found that patients who are hospitalized with COVID-19 have more than double the rate of arrhythmias, including atrial fibrillation and atrial flutter, a similar rapid rhythm that can lead to heart failure and stroke.

Objective: The aim of the study was to evaluate the left atrial structural remodeling in patients with persistent dyspnea and exertional dyspnea post covid 19 infections.

Patients and methods: This case-control study included a total of 60 patients in sinus rhythm, aged > 18 years, attending at Department of Cardiology, Zagazig University Hospitals. They were divided into two groups :(A) included 30 symptomatic subjects recovered from covid 19 who developed exertional dyspnea, compared to group B (30) volunteers without any symptoms. All participants were in sinus rhythm.

Results: Left Atrial (LA) reservoir Strain is decreased in post covid in cases with exertional dyspnea & associated with this dyspnea at odds ratio (OR) of 3.28 (95% CI 1.4 to 7.6), ALSO, LA diameter at OR of 2.7 CI (1.22- 6.77) & p wave dispersion at OR 126 CI (20- 813).

Conclusion: It could be concluded that LAS parameters have a high feasibility to predict symptomatic subjects who developed exertional dyspnea, and fatigue after recovery from covid-19 infection.

Keywords: Left Atrium, COVID-19, Exertional Dyspnea, left atrial strain.

INTRODUCTION

The COVID-19 pandemic has affected more than 170 million people around the world, and previous studies of complications and long-term effects of SARS-CoV-2 infection have found that patients who are hospitalized with COVID-19 have more than double the rate of arrhythmias, including atrial fibrillation and atrial flutter, a similar rapid rhythm that can lead to heart failure and stroke. But exactly how the virus causes these heart complications, has been poorly understood [1].

Myocardial injury in Coronavirus disease 2019 (COVID-19) has been associated with ventricular affection and adverse outcomes; however, associations between atrial affection and arrhythmias, such as atrial fibrillation/flutter (AF) or orthostatic sinus tachycardia, are not well established in this population [2].

Recent advances in two-dimensional echocardiography (2DE), including speckle-based strain, enable the quantification of left atrial strain (LAS), a measure of atrial deformation that has previously been shown to be associated cardiovascular events [3].

The aim of this study was to evaluate the left atrial structural remodeling in patients with persistent dyspnea and exertional dyspnea post covid 19 infections.

PATIENTS AND METHODS

This case-control study included a total of 60 patients in sinus rhythm, aged > 18 years, attending at Department of Cardiology, Zagazig University Hospitals.

The included subjects were divided into two groups; **Group (A)** included 30 symptomatic subjects recovered from covid 19 who developed exertional dyspnea, and **Group (B)** included 30 volunteers without any symptoms.

Inclusion criteria: Post covid-19 patients with residual symptoms (exertional dyspnea, and exercise intolerance) and other control volunteers without symptoms**.**

Exclusion criteria: Patients with valvular heart disease. All sorts of cardiomyopathy, Arrhythmia, Diabetic patients, hypertensive, ischemic heart disease, chronic obstructive pulmonary disease, congenital heart disease, thyroid disease, covid 19 infection with pulmonary embolism.

Patients were subjected to history taking, physical examination, and investigations which included polymerase chain reaction (PCR), complete blood count (CBC) and CRP.

Transthoracic echocardiography:

The echocardiographic examination was performed using a Vivid E9 (General Electric Health Care) ultrasound machine and images were

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acquired with the patient in left lateral decubitus using a 5 MHz transducer at a depth of 15 cm. ECG was recorded, 3 consecutive cardiac cycles of each view were recorded during quiet breathing . All patients were subjected conventional transthoracic echocardiography & Speckle tracking echocardiography (STE). All measurements were taken following the recommendations of the American Society of Echocardiography (ASE) [4].

Left atrium (LA) dimension, and (LV) end-systolic and end-diastolic diameters were measured. LV ejection fraction was estimated by modified Simpson's rule. Left atrial volume index (LAVI), Trans mitral pulsed-wave Doppler velocities were recorded from the apical four-chamber view with the Doppler sample placed between the mitral leaflets tips. Early (E) and late (A) wave peak velocities, E/A ratio, E wave deceleration time (DT), and isovolumetric relaxation time (IVRT) [5].

Tissue Doppler imaging was recorded. The myocardial early diastolic (e`), and late diastolic (a`) velocities were obtained at lateral & septal mitral annuli. The E/e` ratios were subsequently calculated [5].

2D speckle tracking:

Left atrial strain (LAS) analysis was obtained using automated speckle tracking software. The regions of interest (ROI) were generated automatically, and LA endocardial border was manually adjusted when required [6].

LAS values were measured from the LA longitudinal strain curve.LA phases definition and LAS measurement were performed according to the European Association of Cardiovascular Imaging (EACVI)/American society of echocardiography (ASE) guidelines [6].

LAS analysis was calculated with the reference point set at the onset of the QRS complex of the superimposed ECG, the first peak positive deflection corresponds to the value of LAS reservoir function The value of LAS contraction function was obtained .LA strain rate was measured during the early ventricular filling phase).

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

Statistical analyses were performed using SPSS software version 16. Data are expressed as mean standard deviation (SD). The student t test and Chi-square test were used to compare variables between groups. To evaluate the diagnostic performance of left atrial strain and LV diastolic function parameters for the prediction of subclinical cardiac affection, a receiver-operating characteristic curve (ROC) was constructed. Univariate and multivariate Logistic regression analysis were performed to evaluate independent factors associated with predicting subclinical (Diastolic dysfunction). Data were presented as odds ratio (ORs) and 95% confidence intervals (CIs). A statistical test was significant when P value was under 0.05. All P values are the results of 2-tailed tests. P value < 0.05 was considered significant.

RESULTS

Clinical parameters of included patients are illustrated in **table (1).** The mean age of included patients was 32 years and 60% of patients were females. There was statistically significant difference between groups regarding heart rate where higher rate was recorded in symptomatic group (p =0.002). There was no statistically significant difference between both groups regarding other clinical parameters (P<0.05).

Table (1): Clinical characters of included patients

	Overall (N=60)		**Normal (control) (N=30)**		**Symptomatic post covid 19 (N=30)**		**P value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Age (years)	32.6	6.5	32.5	4.7	32.7	8.09	.907
Gender Male	N= 24	40.0%	N= 14	46.7%	N=10	33.3%	.430
Female	N= 36	60.0%	N= 16	53.3%	N= 20	66.7%	
BMI (kg/m^2)	25.95	2.59	1.97	.36	2.98	.544	.057
BSA (m^2)	1.9	0.125	1.88	.097	1.9	0.147	.181
HR	81.5	10.24	70	8.6	88	10.4	**.002**

Table 2 shows that there was statistically significant difference between groups for left atrial strain parameters where symptomatic patients showed lower values with significant difference p =0.000.

Table (2): Left atrial strain parameters

	Normal (control) (N=30)		Symptomatic post covid 19 Patients (N=30)		P value
	Mean	SD	Mean	SD	
LA contraction strain	14.2	5.1	7	24	.000
LA reservoir strain	35.3	9	22.90	8.6	.000
LA diastolic strain	2.40	0.8	2.5	0.8	.09

Table 3 shows that there were positive correlation between post-covid 19 symptoms and CRP, ($p<0.05$), and a negative correlation between post-covid 19 and lymphocytic count ($p<0.05$).

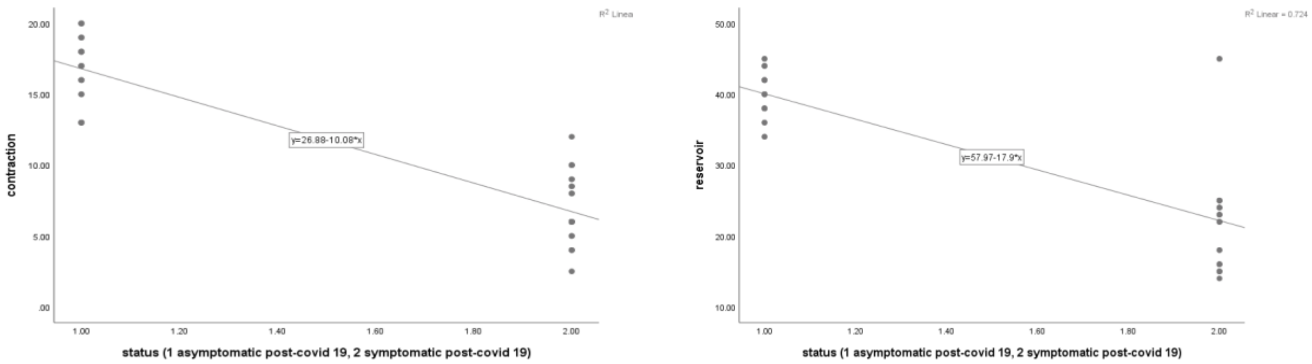
Table (3): Correlation between post covid 19 syndrome dyspnea and baseline characters of included patients

	R	P value
Age (years)	-.017	.895
Sex	.136	.300
CRP (mg/l)	.867**	.000
Lymphocyte (×10^3/ul)	-.869**	.000
Body weight (kg)	.187	.152
BSA (m^2)	.175	.181

There were a positive correlation between post-covid 19 symptoms and E/é sept ($p<0.001$), and IVRT ($p<0.001$). and a negative correlation between post-covid 19 syndrome and left atrial contraction & reservoir strain ($p<0.05$) **(Table 4 figure 1).**

Table (4): Correlation between diastolic parameters and post-covid 19 syndrome

	R	P value
Evel	-.022	.866
EDT	.063	.632
E/é sept	.366**	.004
E/é lat	-.085	.518
E/A	.096	.468
E/SR	.004	.977
IVRT	.744**	.000



(A): LA contraction strain. **(B):** Reservoir strain.

Figure (1): (A and B) Correlation between post-covid 19 syndrome.

The odds for abnormal left atrial strain parameters were increase in symptomatic post covid 19 patients compared with symptomatic post covid 19 patients, In non-adjusted model the odds ratio for LAV index were statistically non-significant while in adjusted model its statically significant ($p<0.05$) **(table 5).**

Table (5): The odds ratio for abnormal left atrial strain parameters regarding post covid 19 syndrome

	OR	95% C.I		P value	aOR*	95% C.I		P value
		Lower	Upper			Lower	Upper	
LADS	2.750	1.224	6.177	.014	52.9	8.200	341.3	.000
LAV index	2	.936	4.273	.074	6.318	1.854	21.527	.003
Reservoir	3.286	1.410	7.657	.006	44.02	8.302	233.5	.000
P wave dispersion	126.0	19.504	813.985	.000	131.	19.134	900	.000

DISCUSSION

The mean age of included patients was 32 years old and 60% of patients were females. There was statistically significant difference between groups for heart rate where higher rate was recorded at symptomatic group ($p = 0.002$). There was no statistically significant difference between both groups regarding other clinical parameters.

In agreement to the present results, **Omar *et al.*** [8] included cases who presented to the cardiology outpatient clinic with persistent chest pain and dyspnea. The subjects had recovered from COVID-19 1-2 months before admission. The median age of cases was 38.5 years ranging between 34 and 46 years. 54% of cases were females, and 46% were males. The mean BMI 25.19 kg/m^2 (23-28.3).

In contrast to the present study regarding age and gender distribution, **Young *et al.*** [9] in their study conducted on total of 259 individuals had both a baseline echocardiogram prior to their COVID-19 diagnosis and an outpatient echocardiogram completed after recovery from COVID-19 infection. The average age of patients included was 60 years (SD 16), 47% were female, 53% were males. The mean BMI was 30 kg/m^2.

Erdol *et al.* [10] found that 16% of cases were asymptomatic and 84% were symptomatic. The mean age of the patients in the study was 35 (range: 19–39 years) and 55% were male, and 45% were females. 22% of cases had dyspnea.

The present findings showed impaired LA strain parameter (reservoir & contraction) in symptomatic group as compared to asymptomatic group. LA strain reservoir in asymptomatic patients was 35.3 and contraction was 14.2 compared with symptomatic patients' reservoir was 22.9 and contraction was 7. There was statistically significant difference between groups at left atrial strain parameters where symptomatic patients showed lower values with significant difference P =0.000.

In contrast to the present findings, **Beyls *et al.*** [7] stated that the symptomatic cases had the median left atrial strain during reservoir phase (LASr) was 30.5%, left atrial strain during contraction phase (LASct) was -13.3%.

In the current study, there was a significant association between post-covid 19 symptoms and E/é sept ($p<0.001$), and IVRT ($p<0.001$), and left atrial contraction & reservoir strain ($p<0.05$).

Several studies suggested that impaired LA reservoir function may be a sign of LA remodeling, caused by several cardiovascular conditions, such as hypertension, diabetes or ischemic heart disease[10-11].

LAS reservoir parameter is also a prognostic factor for the occurrence of AF in ischemic stroke, heart failure or after cardiac surgery and reflects LA compliance [12].

Multiple researchers studied LA strain and its association with adverse outcome in covid-19 patients.

As reported In **Beyls *et al.*** [7] study, LAScd was a strong predictor of AF and the identified cutoff value of − 11% was closed to that of previously observed cutoff in different cardiovascular disease. For example, in Chagas disease, the LA conduit function (−12.6±5.7%) was reported to be a strong predictor of AF due to the depression of the LA conduit function[13] .

In **Beyls *et al.*** [7] study, LASr values were significantly impaired in covid-19 AF group 30.5 [23.8–36.2] % vs. 20.2 [12.3–27.3] %; *P*=0.002).

In our study we evaluated the predictive value of LA strain of the developed dyspnea and exercise intolerance post covid-19 recovery. In symptomatic patients LA strain reservoir was 22.9±8.6 and contraction was 7±2.4 while in asymptomatic patients LA strain reservoir was 35.3±9 and contraction was14.2±5.5.

In line with the present study **Goerlich *et al.*** [14] reported similar LASr values (30.4 [26.1–35.8] % vs. 22.3 [20.6–27.8] %; P<0.001) in symptomatic versus normal cases and shown that LASr parameter was an independent factor of AF in COVID-19 patients.

CONCLUSION

It could be concluded that LAS parameters have a high feasibility to predict symptomatic subjects who developed exertional dyspnea and exercise intolerance after recovery from covid-19 infection. Hence, the present study emphasizes the fact that LAS analysis can be easily performed in patients using a dedicated mode for LAS analysis and an automated approach as recommended.

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