Speckle Tracking Echocardiography in Post Covid 19 Recovered Patients

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Abstract

Background: Speckle tracking echocardiography represents an advanced, noninvasive imaging modality that allows a fast and accurate assessment of the global and regional function of both atrial and ventricular chambers, independently from the angle of insonation and in-plane translational motion. STE is based on the interaction between the myocardial tissue and the ultrasound beam that produces particular acoustic markers.

Objective:To assess left atrial strain and strain rate in patients recovered from COVID-19.**Conclusion:**COVID-19 may unmask subclinical Left Atrial (LA) dysfunction or exacerbate preexisting LA dysfunction. Moreover, recent findings suggested that COVID-19 patients with severe respiratory failure had a high prevalence of increased LVEDP. However, data about the potential effect of COVID-19 on LAcd function are currently lacking.

Keywords: Speckle tracking echocardiography (STE), COVID-19, Left Atrial (LA) , Atrial fibrillation (AF)
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Introduction

Since its emergence in 2019, more than 227 million SARS-CoV-2 infections have occurred worldwide, with more than 4.6 million fatalities. Despite exhibiting proofreading activity, coronaviruses mutate frequently[1].

Leading to thousands of mutations among the different strains. The most crucial mutations have involved the spike protein, which mediates binding to the angiotensin-converting enzyme 2 (ACE2) receptor via its S1 domain and membrane fusion via the S2 domain[2].

Spike substitutions influence host range, tissue tropism, transmission and pathogenesis[3].

SARS-CoV-2 as well as SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) cause severe pneumonia with a fatality rate of 2.9%, 9.6% and ~36%, respectively. The other four human coronaviruses, OC43, NL63, HKU1 and 229E, generally cause self-limited disease with mild symptoms[4].

Speckle Tracking Echocardiography:

Speckle tracking echocardiography (STE) is an echocardiographic technique with an exponentially increasing clinical application since its first introduction[5].

Speckle tracking echocardiography represents an advanced, noninvasive imaging modality that allows a fast and accurate assessment of the global and regional function of both atrial and ventricular chambers, when blood fills the left atrium, as a conduit in early diastole corresponding to passive left ventricular filling and as an active contractile chamber in late diastole[8].

Strain analysis has been utilised for evaluation of LA function. Strain evaluates myocardial deformation while strain rate examines the rate of change in strain, and can be measured throughout the cardiac cycle, thereby enabling the evaluation of LA reservoir function (in systole) and conduit and contractile function (in diastole) [9]. .

Strain and strain rate imaging of the LA

Strain and strain-rate imaging have several advantages over conventional echocardiography in evaluation of LA function. Firstly, strain imaging is not evaluated relative to the transducer position, thus allowing discrimination between active and passive myocardial tissue movement. Strain parameters are relatively independent of tethering effects and is less load dependent compared to traditional parameters of LA function. Additionally, strain and strain rate parameters permit evaluation of phasic atrial function throughout the cardiac cycle[10].

Types of LA strain modalities:

LA strain measurements can be obtained by tissue Doppler imaging (TDI), two-dimensional (2D) speckle tracking echocardiography (STE) and velocity vector imaging (VVI). For the latter two techniques, longitudinal strain and strain rate curves are generated for each of six atrial segments, obtained from the apical four and two chamber views (Figure 1). Heterogeneous segmental deformation of the LA has also been observed, with higher values noted in the regions adjacent to the mitral annulus[8].

independently from the angle of insonation and in-plane translational motion. STE is based on the interaction between the myocardial tissue and the ultrasound beam that produces particular acoustic markers[6].

It is possible to identify several advantages of STE-derived strain analysis in comparison with previous methods which were based on tissue Doppler imaging, a technique that is currently rarely used. The main benefits include the capability to evaluate the two-dimensional (2D) displacement of cardiac muscle spots during the cardiac cycle and to calculate, in an angle-independent way, the myocardial deformation through the distance variation between the speckles in the analyzed segment. For the first time in a 2D echocardiographic modality, it is possible to obtain a reconstruction of the spatial deformation of left ventricular (LV) myocardium along different spatial planes: longitudinal, radial, circumferential, and rotational[7].

Left Atrial Strain:

Left atrial function: evaluation by strain analysis:

The left atrium has an important role in modulating left ventricular filling, contributing up to a third of cardiac output. The left atrium has additionally been identified as an important biomarker of cardiovascular disease and adverse cardiovascular outcomes. While previously left atrial (LA) size was utilised, the role of LA function as a biomarker is increasingly being evaluated, both independently and also in combination with LA size. However, LA function is complex, comprising of three main components: reservoir function in systole

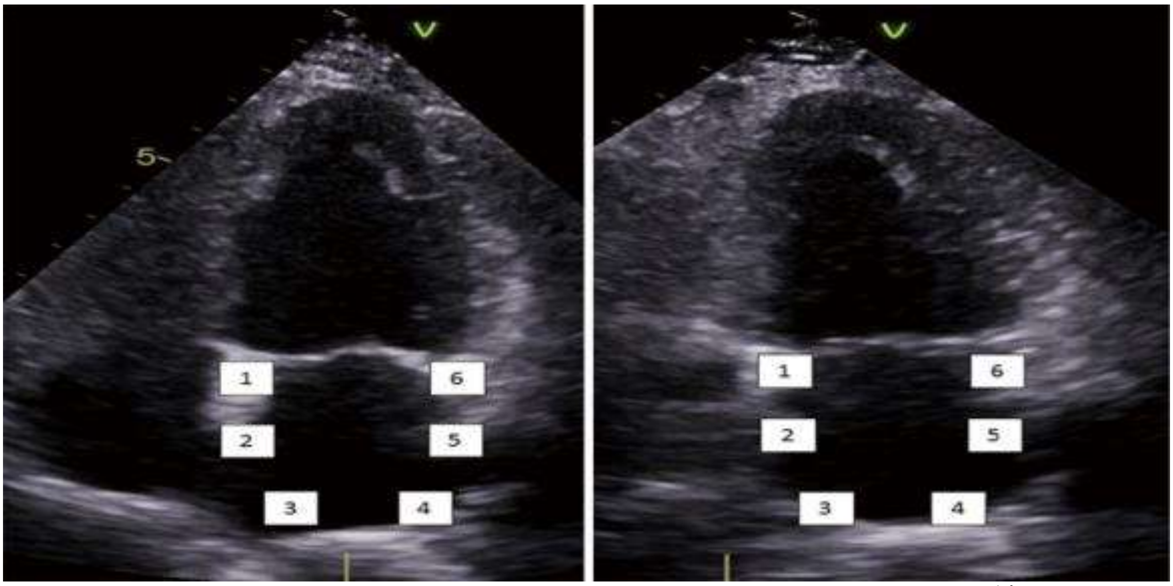

Figure (1): Apical four and two chamber six LA segments. LA, left atrial [8].

In the reservoir phase, as the LA fills and stretches, there is positive atrial strain that reaches its peak in systole at the end of LA filling, prior to opening of the mitral valve. Following this, passive LA emptying ensues with opening of the mitral valve resulting in decreased atrial strain with negative deflection of the strain curve up to a plateau period which is analogous to diastasis. A second deflection in the strain curve is then observed corresponding to atrial systole. Peak atrial longitudinal strain (PALS) or LA systolic strain is measured at the end of the reservoir phase. Peak atrial contraction strain (PACS) or late diastolic strain, is measured following the P wave and corresponds to active atrial contraction (Figure 2) [11].

1- 2D speckle tracking derived LAS:

Apical four and two chamber view images of the LA are obtained using conventional 2-dimensional echocardiography, at relatively high frame rates (60–80 fps). The LA endocardium is traced in both four and two chamber views and the ROI adjusted to the thinner wall of the atrium. In regions of discontinuities of the LA wall, such as areas corresponding to pulmonary veins and LA appendage, extrapolation of the LA endocardial and epicardial surfaces at the junction of these structures are performed to obtain the ROI. The ROI is divided into six segments and the total of 12 segments is analysed with the software generating the individual segmental longitudinal strain curves together with global strain in each view (Figure 2) [9].

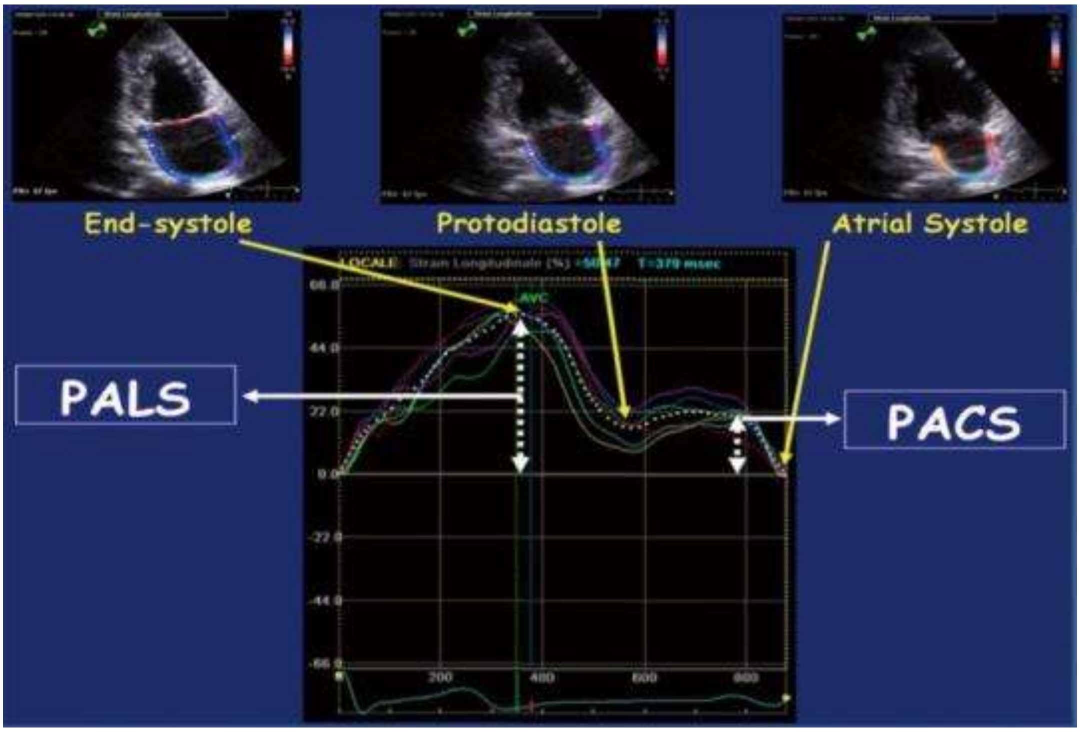

Figure (2): Peak atrial longitudinal strain (PALS) and peak atrial contraction strain (PACS)[11].

LA strain curves have two patterns that differ based on the time in the cardiac cycle from which the software processing begins i.e., either at the onset of the P wave (atrial cycle/diastolic gating) or the onset of the QRS complex (ventricular cycle/systolic gating). If the strain processing begins at onset of QRS, ventricular end diastole is the zero reference and peak positive longitudinal strain corresponds to atrial reservoir function, strain during early diastole reflects atrial conduit function and strain during late diastole corresponds to atrial contractile function, Conversely, if software processing begins at onset of P wave, atrial end diastole becomes the zero reference and the first negative peak strain represents the atrial contractile function, positive peak strain corresponds to conduit function, and their sum (strain total) represents reservoir function,Strain rate in ventricular systole (S sr), early diastole (E sr) and late diastole (A sr) correspond to reservoir, conduit, and booster pump functions in both methods[11].

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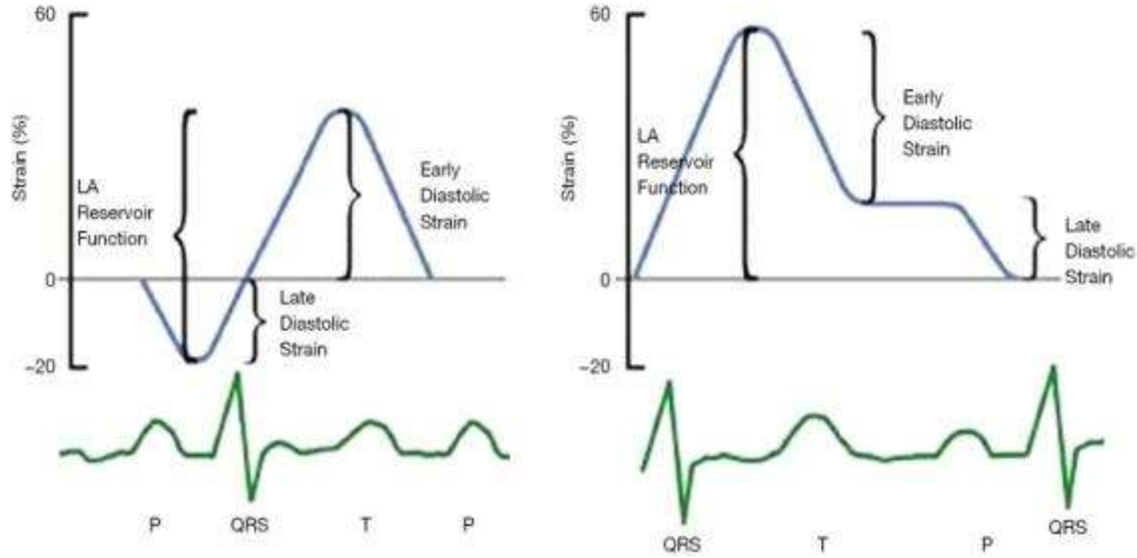

Figure (3): Strain trace based on choice of electrocardiographic gating; electrocardiographic P wave used on the left and QRS complex used on the right[8]

as the reference than when the QRS onset was used. Nevertheless, as timing of reference point selection has not been uniformed in studies to date, no standardised method for LA strain analysis has yet been proposed.

Hayashi et al.[12] showed that the degree of correlation between LA strain and parameters of LA function determined by three-dimensional echocardiography were stronger when the onset of P wave was used

Table (1): Left atrial strain indexes and reference values[13]

Parameter	Reference values(mean±SD)
Global LA-RS%	42.2%±6.1
LA contractile strain	13.9±3.6
LA conduit strain	21.9±9.3

Abbreviations: LA-RS = left atrial reservoir strain.

strain rate during late diastole (i.e., PACS) to be −2.11±0.61 s^{-1}. The lowest expected values (using mean −2 SD) was 23.1% for LA systolic strain and −0.91 s^{-1} for A sr in late diastole[14,15].

Reference values for LA strain and strain rate have been reported. In a multicentre study involving 329 healthy subjects, Morris et al. reported LA systolic strain (i.e., PALS) to be 45.5%±11.4% and LA

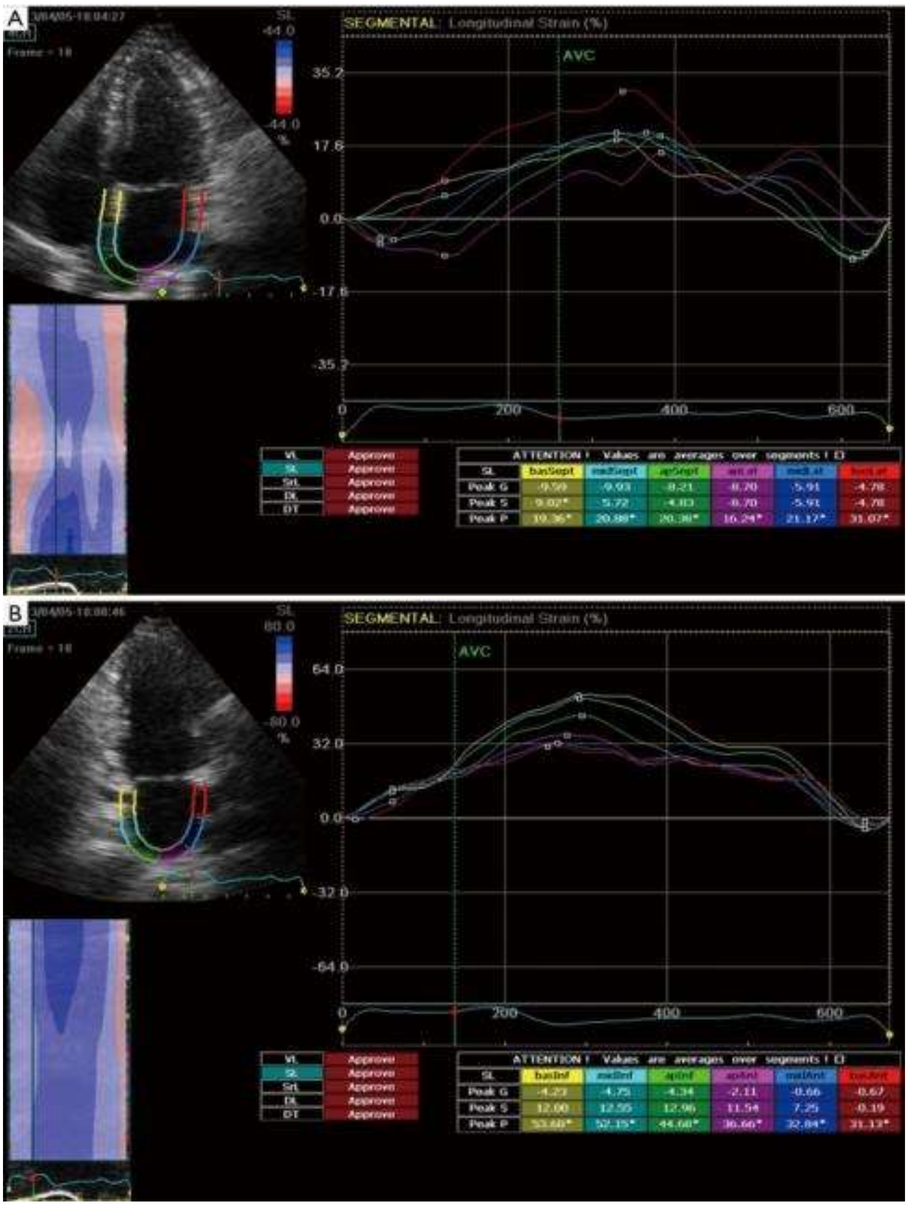

Figure (4): 2D strain by speckle tracking echocardiography demonstrating segmental and global LA strain from the apical (A) four and (B) two chamber views. LA, left atrial[9].

narrow sample volume (9 mm × 1 mm) is selected due to the thin atrial walls, as compared with the sample volume used for LV strain measurements (9 mm × 9 mm). The sample volume is placed superiorly in each of the four LA walls; septal and lateral walls in the apical four chamber view and the inferior and anterior walls in the apical two chamber view. The sample volume is then tracked frame by frame, within this position in the LA

2-LA strain by TDI:

TDI depicts myocardial motion (measured as tissue velocity) at specific locations in the heart. Integration of velocity over time yields displacement or the absolute distance moved by that point. Tissue-Doppler LA strain and strain rate are measured offline from colour tissue Doppler images of the atria obtained in the apical four and two chamber views, at high frame rates (>100 fps). A by adjusting the electrocardiogram gating to the start of the QRS complex (systolic gating) (Figure 5). Atrial strain rate was measured in S sr, E sr and Asr (Figure 6) [16].

wall, to prevent sampling of blood pool. The superior location in the LA walls is selected to avoid interference from mitral annular motion. Peak LA systolic strain was measured

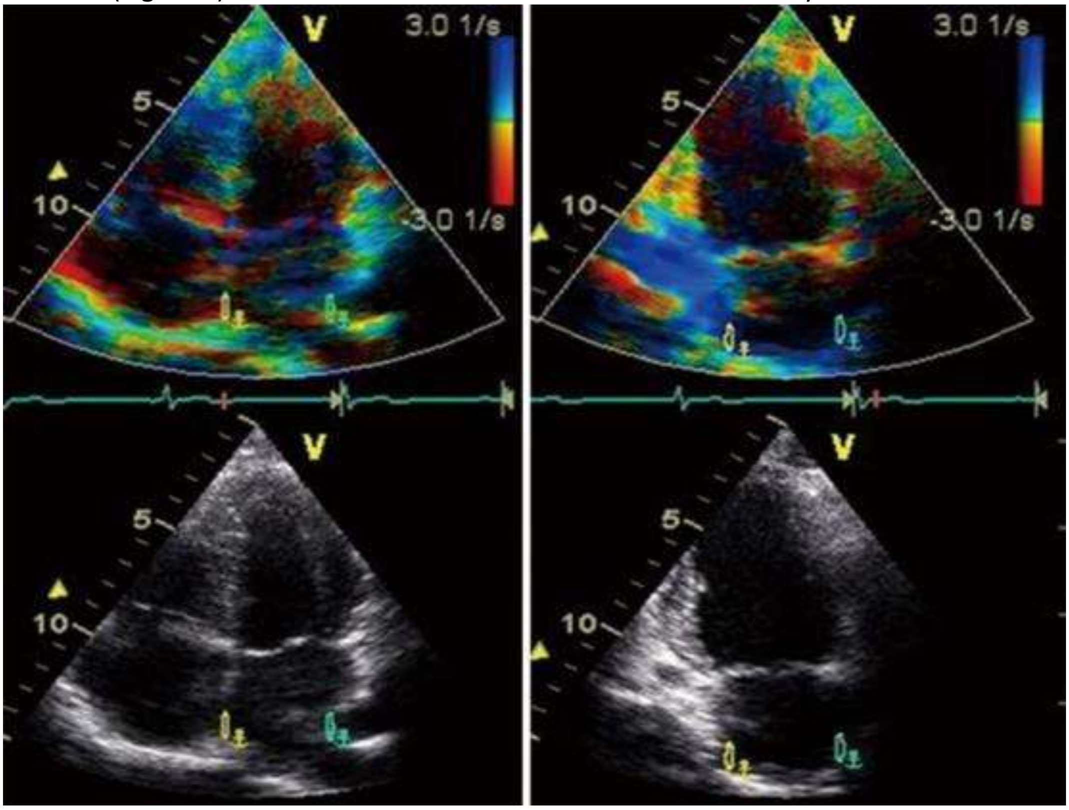

Figure (5): Peak systolic strain measured by ECG gating to the start of the QRS complex (systolic gating) [17].

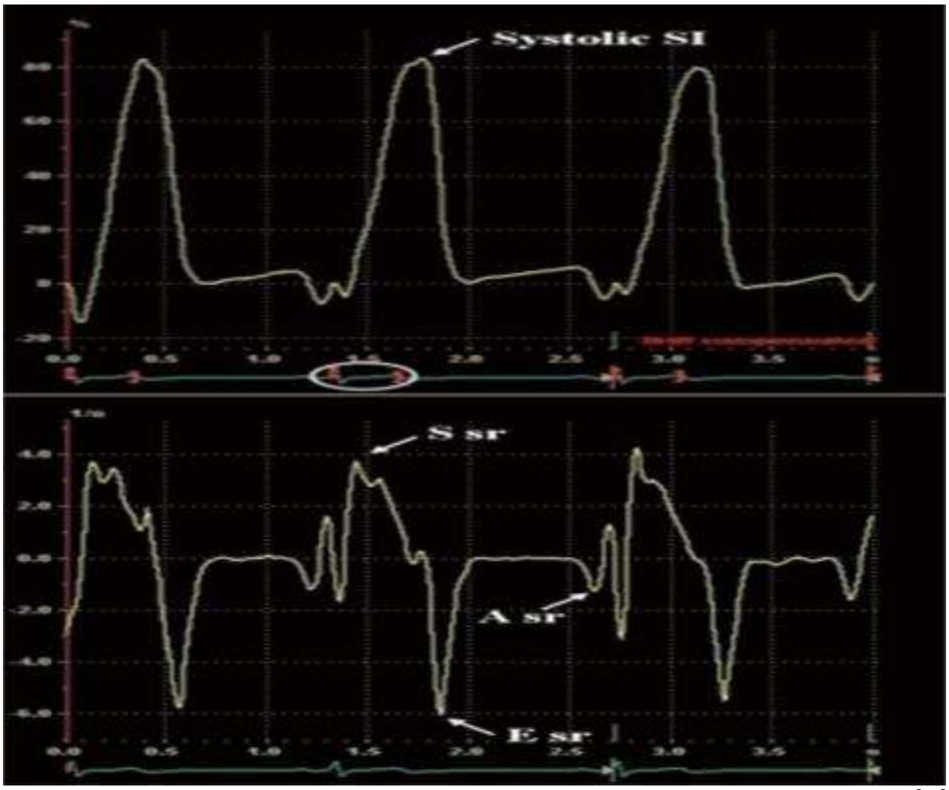

Figure (6): Atrial strain rate measured in systole (S sr), early (E sr) and late diastole (A sr) [17].

advantages of simpler and faster tracking/processing times compared to conventional STE with the use of a continuously self-updating software and requires only a single frame tracing of the endocardialborder[17].

With VVI analysis, 2D images of apical four and two chamber views are obtained with recommended frame rates between 70–100 Hz. The endocardium of the LA is manually traced in the four and two chamber views and velocity vectors are generated in cine loop format. The ROI is delineated and tracked. The displacement of LA endocardial pixels of the ROI and the velocity of deformation in every frame with the elongation or shortening of myocardium throughout the cardiac cycle, are the strain and SR measures which are calculated automatically (Figure7). Special reference settings are applied, including valve annulus, chamber borders and tissue motion[20].

TDI LA strain also has demonstrated prognostic value. Decreased LA systolic strain has been associated with increased LV end-diastolic pressure and is thus, a predictor of diastolic HF. LA TDI strain has also been shown to be an important predictor of maintenance of SR following both cardioversion and ablation for AF[18].

TDI LA strain has been used to demonstrate reduced reservoir and conduit phasic function with preserved active contractile function in patients with metabolic syndrome. The use of tissue Doppler techniques in this cohort may have been of particular importance in the setting of potential suboptimal 2D image quality[19].

3-LA strain by VVI:

Vector velocity imaging is a novel echocardiographic method that combines speckle tracking and endocardial border detection. Similar to 2D STE strain imaging, VVI is angle independent but has additional

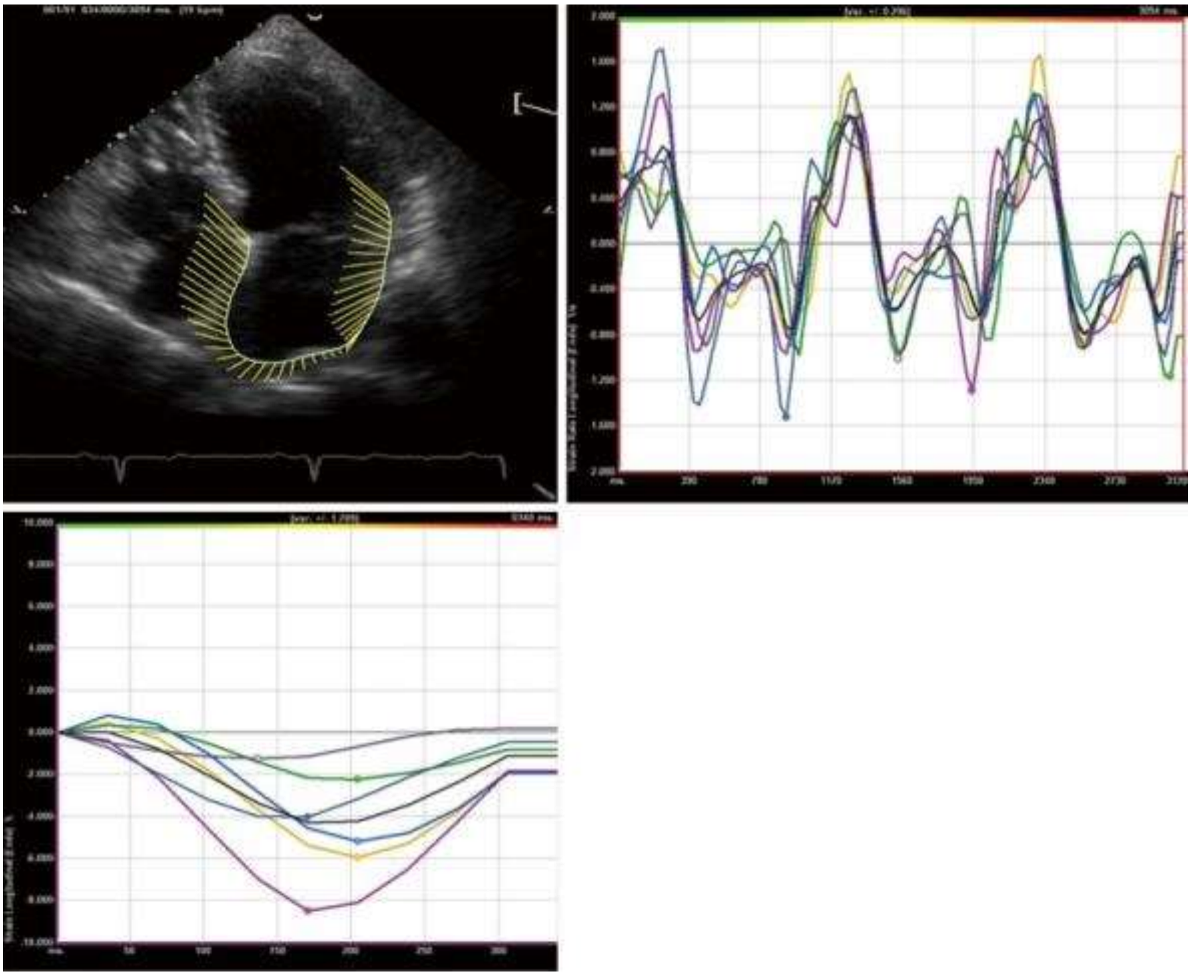

Figure (7): Velocity vector imaging[21].

comparable strain and strain rate measurements using the two techniques[22].

LA strain in COVID-19 patients:

Among patients with cardiac disease and COVID-19 pneumonia, atrial fibrillation was the most common documented arrhythmia with an incidence up to 36%[23].

New-onset AF is associated with increased mortality in critically ill patients and is strongly associated with mechanical ventilation, organ failure and norepinephrine use[24,25].

Thus, prediction of AF risk is important. In the study of Beyls and coworkers, 20% of patients admitted to the Intensive Care Unit because of COVID-19

VVI has been shown to be feasible and less time consuming in assessing LA volumes and function. In a study by Valocik et al. retrospectively assessing 100 transthoracic echocardiograms, LA volumes derived from VVI time volume curves had a good correlation with conventional LA volume assessment. A moderate level of correlation was noted with respect to LAEF. VVI led to a 62% reduction in measurement time in comparison to conventional 2D assessment[21]. These findings were corroborated by Motoki et al. in a separate study involving 127 patients with AF. Measurement of LA strain and SR by VVI and 2D STE was noted to be feasible in a large proportion of patients with

et al[30]reported an in-hospital mortality of 39.2% (n = 65/166) in COVID-19 patients with AF and showed that AF was an independent predictor of in-hospital mortality. However, in this report only 60% of patients with AF were hospitalized in ICU.

AF and critical ill:

AF is a common complication of critical illness and is an independent predictor of mortality. In septic patients, mechanical ventilation, organ failure and norepinephrine use were strongly associated with AF[24]**.** In **Beyls et al**[25] **(2021)** study, norepinephrine use was strongly associated with AF to the contrary to mechanical ventilation. However, AF was not associated with 30-day mortality (43% vs. 22%; P = 0.11) probably due to a lack of statistical power explained by the limited sample size.

AF and LA strain function:

LAS reservoir parameter is also a prognostic factor for the occurrence of AF in ischemic stroke, heart failure or after cardiac surgery **Pessoa-Amorim et al**[31]and reflects LA compliance[32]**.** 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[33]**.** In **Beyls et al**[30]study, LASr values were significantly impaired in the AF group 30.5 [23.8–36.2] % vs. 20.2 [12.3–27.3] %; P = 0.002). **Goerlich et al**[34]reported similar LASr values (30.4 [26.1–35.8] % vs. 22.3 [20.6–27.8] %; P < 0.001) and shown that LASr parameter was an independent factor of AF in COVID-19 patients. However, in **Beyls et al**[30] study, only LAScd remained independently associated with AF probably due to the limited sample size of their cohort.

Clinical data on LA mechanistic dysfunction suggested a strong link between left ventricular diastolic dysfunction and risk of AF[35]**.**

pneumonia developed new-onset AF. LA reservoir and conduit strain values were significantly impaired in the AF group with COVID-19 pneumonia; however, only LA conduit strain remained independently associated with AF[25]**.**

Furthermore, **Beyls and coworkers**[25]reported a cut-off value of -11% for LA conduit strain to predict new-onset AF in COVID-19 pneumonia with a sensitivity of 76% and a specificity of 75%.

Atrial fibrillation (AF) is frequent in critically ill with an incidence varying from of 1.9 to 43.9% and is associated with a substantial morbidity and mortality. For patients suffering from COVID-19, AF is the most frequently documented arrhythmia with an incidence between 19 and 36% according to the current literature and seems to be higher in non-surviving COVID-19 patients[23,26]**.**

The involvement of COVID-19 infection in the development of AF is probably due to several complex physiopathological mechanisms and triggers, such as hypoxemia, systemic inflammation, electrolyte abnormalities or alteration of the renin–angiotensin aldosterone system. Moreover, patients with AF and patients with COVID-19 share common risk factors and cardiac comorbidities, such as age, obesity or high blood pressure[27]**.**

AF and critical COVID-19 patients:

Recent findings supported the higher likelihood of observing AF in COVID-19 patients admitted to the ICU. Moreover, AF may worsen the clinical evolution of pneumonia in these patients[28,29] reported an AF prevalence of 16.5% in ICU patient and showed that mechanical ventilation was strongly associated with AF. Here, **Beyls et al**[25]reported comparable results as 20% of their patients developed AF during ICU stay and AF was strongly associated with a more critical state (69% vs. 22%; P < 0.0001). **Pletzer**

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LAS analysis, especially left atrial strain conduit function (LAScd), has recently emerged as a powerful tool for left ventricular diastolic dysfunction evaluation**Fan et al. [36]**especially when left ventricular end diastolic pressure (LVEDP) was increased**[37].** Severe hypoxemic COVID-19 pneumonia may be associated with diastolic dysfunction and/or increased LVEDP. Indeed, COVID-19 infection can lead to myocardial diastolic dysfunction**Freaney et al[38]** by direct virus related-myocardial injury, inflammation or cardiac fibrosis[39].

COVID-19 may unmask subclinical LA dysfunction or exacerbate preexisting LA dysfunction**[40].** Moreover, recent findings suggested that COVID-19 patients with severe respiratory failure had a high prevalence of increased LVEDP**[41].** All these elements may lead to AF. However, data about the potential effect of COVID-19 on LAcd function are currently lacking and further studies on the subject would be of great interest.

Conclusion:

In conclusion,we found a high feasibility of LAS parameters to predict persistent symptomatic in subjects who developed exertional dyspnea, fatigue 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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