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### Relation Among Right Ventricular Dysfunction, Lung Damage, and Mortality in Patients With COVID-19



We read with interest the paper by Li et al. (1), which evaluated the prognostic value of speckle-tracking echocardiography derived right ventricular longitudinal strain (RVLS) in 120 hospitalized patients with coronavirus disease 2019 (COVID-19). The authors confirmed that impaired RVLS was associated with the mortality, but 3 key issues deserve further consideration.

First, a confounding bias. Right ventricular (RV) function is closely linked with afterload. The same is applicable for RVLS, which is modulated by afterload. Although RV dysfunction can be induced by direct COVID-19 damage, a more likely scenario is that it results from severe lung damage, including the development of acute respiratory distress syndrome and pulmonary hypertension. As the authors showed, there was no association between the cardiac enzyme (creatinine kinase myocardial band, High-sensitivity Troponin I, and B-type natriuretic peptide) and RVLS, but patients with impaired RVLS had more tricuspid regurgitation and higher pulmonary artery systolic pressure than those without impaired RVLS. As such, given the small number of events, it becomes impossible, in our view, to claim with certainty that RVLS is independently associated with outcomes in this sick group of patients without properly accounting for the health of the right-side unit (2). This includes incorporating the right chamber size (larger in nonsurvivors), pulmonary pressures (greater in nonsurvivors), tricuspid regurgitation severity, and RV systolic function. Given the small number of events, the authors could at minimum evaluate the impact of the RV-PA coupling, which takes into account RV systolic performance at a given degree of afterload and which has been shown in several other cohorts to be prognostically important (3,4).

Second, the incremental prognostic value of RVLS over the comprehensive clinical assessment including known risk factors is also unclear, which given a likely type II error (underpowered), becomes less apparent. A case in point is baseline cardiovascular disease, which has a significant hazard ratio in the univariate analysis (2.93) and is shown by many other

publications in this COVID-19 population to be associated with worse outcomes, but “loses” its significance in the overfitted multivariate model (3 variables for 18 events).

Last, RVLS is highly dependent on adequate image quality, which can be challenging in this group of sick patients, at times in the intensive care unit on mechanical ventilation or in supine or prone position, all of which make echocardiographic imaging quality decrease. In fact, the authors excluded 24 (16%) of the initial 150 patients, due to suboptimal image quality analysis for RVLS. Could other parameters of RV size/function be assessed besides RVLS in these excluded patients?

The study by Li et al. (1) is an important first step in the assessment of RV dysfunction in patients with COVID-19, and we commend them for exploring new parameters of RV performance. However we believe that a more balanced perspective of their findings is necessary, because we do not know the additional value of RVLS over the other clinical and echocardiographic parameters, which can be assessed more easily and possibly without direct potential exposure to COVID-19. Further studies are needed before this parameter could be used to improve the risk stratification.

Miho Fukui, MD, PhD

João L. Cavalcante, MD\*

\*Cardiac MRI and Structural CT Labs

Minneapolis Heart Institute

Abbott Northwestern Hospital

Cardiovascular Imaging Center and Core Lab

Minneapolis Heart Institute Foundation

920 East 28th Street

Suite 100

Minneapolis, Minnesota 55407

E-mail: [Joao.Cavalcante@allina.com](mailto:Joao.Cavalcante@allina.com)

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## Right Ventricular Longitudinal Strain

A New Prognostic Tool for COVID-19?



We have read with interest the recent paper by Li et al. (1) regarding the prognostic value of right ventricular longitudinal strain in patients with coronavirus disease 2019 (COVID-19) (1). As the morbidity and mortality of the ongoing pandemic COVID-19 are posing a serious threat to health care systems all over the world, the urge to find prognostic factors to better stratify patients and offer an adequate level of medical assistance to everyone is of the utmost importance.

However, we have some remarks, both from a clinical and methodological point of view.

First, the authors report a remarkable incidence of deep vein thrombosis (DVT) (41% of the population), with surprisingly no documented cases of pulmonary embolism (PE). We wonder how the diagnosis of DVT and PE was performed (i.e., was there an extensive screening protocol for both DVT and PE?) and how these findings were interpreted by the authors. Do the authors think that eventually undiagnosed or sub-clinical PE events may explain right ventricle (RV) echocardiographic parameters modification in patients with bad prognosis?

A methodological remark regards the significant variability of the timing of the echocardiographic study, with an interquartile range of 3 to 10 days between admission and examination. We wonder if this could have affected the results, possibly increasing the prognostic values of RV dysfunction for tests performed during the detrimental phase of ARDS. Moreover, it should be stated if echocardiography was performed during invasive or noninvasive ventilation or in oxygen, as it is well known how ventilation itself could significantly modify echocardiographic parameters, including RV longitudinal strain (2). This could represent a potential bias, as severe patients were more likely to undergo ventilation support, a condition that possibly makes RV echo parameters just innocent bystanders.

Finally, the proposed cutoff values for right ventricular longitudinal strain, (RVLS) tricuspid annular plane systolic excursion (TAPSE), and right ventricular fractional area change (RVFAC) are largely within the normal range in healthy subjects. We wonder how the authors interpreted the biological plausibility of their findings. Is it possible to speculate that the active phase of the disease leads to a form of “overload” of the RV, where the inability to

overcompensate (resulting in increased RV systolic function parameters) carries a worse prognosis?

Riccardo Schiavon, MD\*

Giovanni Casazza, PhD

Chiara Cogliati, MD

\*Emergency Medicine Department

L. Sacco Hospital

Via G. B. Grassi 74

20157 Milan

Italy

E-mail: [schiavon.riccardo@asst-fbf-sacco.it](mailto:schiavon.riccardo@asst-fbf-sacco.it)

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## THE AUTHORS REPLY:



We appreciate the comments by Dr. Fukui and colleagues about our paper (1), and we fully agree with some of their views. However, there are some issues that need to be clarified and discussed.

We acknowledge and agree that right ventricular (RV) function is closely linked with the afterload. In our cohort study, 40 (34.2%) patients developed acute respiratory distress syndrome (ARDS), which contributed to increase RV afterload. Furthermore, both ARDS and right ventricular longitudinal strain (RVLS) were found to be associated with mortality, consistent with the previous study (2).

It is difficult for us to evaluate the right ventricular to pulmonary artery (RV-PA) coupling by measuring a ratio between tricuspid annular plane systolic excursion and pulmonary artery systolic pressure (PASP), as suggested by Cavalcante (3). Noninvasive PASP measurement depends on the presence of tricuspid regurgitation (TR), and there were only 61 patients (50.8%) had interpretable TR jet signal in our study. Among them, the majority was mild or trivial TR, which may affect the accuracy of PASP assessment. As the right heart catheterization was not available in our designated treatment hospital, PASP derived from