Coronavirus Disease 2019: There Is a Heart Between the Lungs*

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As of April 30, 2021, over 150 million people have contracted the coronavirus disease 2019 (COVID-19). If many have no or mild flu symptoms, some develop complications. The most common complication is a pneumonia that may become an acute respiratory distress syndrome (ARDS) and require ICU admission and mechanical ventilation for weeks. In severe COVID-19 cases, hemodynamic instability is not uncommon. Around two third of ICU patients require vasopressor support (1). Multiple factors may explain hemodynamic disturbances in patients with COVID-19. Vasodilation may be induced by systemic inflammation, sedative drugs during mechanical ventilation, and bacterial superinfection. Hypovolemia may be a factor contributing to hemodynamic instability. Many patients had or have fever, and fluid restriction is often the rule, as soon as patients become hypoxemic, in order to limit the development of pulmonary edema. Circulating proinflammatory cytokines and/or the infection of myocardial cells by the coronavirus may impair both right and left ventricular (LV) systolic function. In patients with ARDS, pulmonary capillary microthrombi, hypoxic pulmonary vasoconstriction, and mechanical ventilation with a high positive end-expiratory pressure may impede right ventricular (RV) ejection. The above-mentioned mechanisms may be intricated and can be detected by a point of care ultrasound (POCUS) evaluation (2, 3).

RV DYSFUNCTION IN COVID-19

In this issue of *Critical Care Medicine*, Chotalia et al (4) reported echocardiographic findings in 172 mechanically ventilated COVID-19 patients with ARDS. The ultrasound evaluation was mostly triggered by hemodynamic instability or by an increase in troponin. A RV dilation, defined as a RV/LV end-diastolic area ratio greater than 0.6, was observed in 49%. A RV systolic dysfunction, defined as a RV fractional area change (FAC) less than 35%, was as common (51%). Previous studies have shown that around 30–40% of COVID-19 inpatients have echocardiographic signs of RV dysfunction (2, 3). The higher prevalence of RV dysfunction reported by Chotalia et al (4) is not surprising given the focus on mechanically ventilated patients with ARDS. Their findings are consistent with the results of previous studies done in patients with ARDS not related to COVID-19 (5, 6).

Mortality was higher in patients with RV dilation (49% with vs 33% without), as well as in patients with RV systolic dysfunction (53% with vs 28% without). In the multivariate analysis, only the association of dilation and systolic dysfunction was significantly associated with mortality, with an odd ratio at 3.11, and a broad

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CI ranging from 1.15 to 7.60. Previous but smaller studies done in COVID-19 patients had already reported a significant association between RV dysfunction and mortality (7, 8). Whether RV systolic dysfunction may be responsible for a decrease in oxygen delivery to the tissues, organ failure, and death remains unclear. RV dysfunction may simply be a marker of lung disease severity, as suggested by the significant relationship observed between RV FAC and the PaO_2/FIO_2 ratio, the compliance of the respiratory system, and chest radiograph abnormalities. Regrettably, Chotalia et al (4) did not quantify cardiac output. It would have been interesting to know if RV systolic dysfunction had an impact on systemic blood flow and if cardiac output was also associated with mortality.

To assess RV systolic function, Chotalia et al (4) assessed the RV FAC and the tricuspid annular plane systolic excursion (TAPSE). Eyeballing and TAPSE are the most widely used methods to assess RV function (9). TAPSE was normal in 81% of patients with a decrease in FAC (< 35%). Conversely, none of the patients with a low TAPSE (< 17 mm) had a normal FAC (> 35%). In other words, the assessment of TAPSE did not add anything to the assessment of RV FAC. These findings are consistent with the results of previous reports done in patients with septic shock (10) and in patients with COVID-19 (11).

THE RISE OF POCUS EVALUATIONS IN COVID-19 PATIENTS

The use of POCUS sharply increased since the beginning of the pandemic, in particular to detect lung abnormalities. Pulmonary consolidations and pleural effusion can be visualized at the bedside in a few minutes, whereas CT scans are time consuming and must be done in the radiology department. Pulmonary edema can be detected and estimated by counting the number of B lines. In the ICU, ultrasounds are also increasingly used for vascular access and to assess the diaphragmatic function, particularly during weaning from mechanical ventilation. A large international survey (12) of clinicians involved in the treatment of COVID-19 ICU patients showed that echocardiography was used by a majority of respondents to assess biventricular systolic function and to measure cardiac output. According to the survey, ultrasounds were also used to predict fluid responsiveness by 62% of respondents, that is, more often than the pulse pressure variation (46%) or the passive leg raising maneuver (45%).

The rise in POCUS evaluations may be explained by the growing number of training programs and both hardware and software innovations. In the past, echocardiographic evaluations were done in carefully selected ICU patients by cardiologists who often had to bring the heavy ultrasound machine from their department. Things dramatically changed over the last decades (13). POCUS evaluations are increasingly done by intensivists who received a specific training, with a focus on the evaluation of shock states. Cart-based ultrasound systems are much smaller and easy to move from one ICU room to the other. Miniaturized echo devices started to replace the stethoscope in the pocket of an increasing number of clinicians (**Fig. 1**). Although pocket tools do not have all the functionalities offered by bigger cart-based systems, they have the advantage to enable quick qualitative POCUS evaluations. They are also affordable, contributing to their adoption in low- and middle-income countries.

Besides the above-mentioned form factors that may profoundly impact clinical adoption, multiple software innovations have been proposed to help clinicians get the most of ultrasound images. Some have been designed to help clinicians measure specific variables, for example, the subaortic velocity time integral or the respiratory swings in the inferior vena cava diameter (Fig. 1). Speckle tracking or strain echocardiography enables the automatic and visual assessment of myocardium shortening during systole (Fig. 1). Studies have suggested that the RV global longitudinal strain and the RV free wall longitudinal strain are better markers of systolic function than FAC and TAPSE (14). Unfortunately, Chotalia et al (4) did not postprocess their images with a speckle tracking software. Therefore, we do not know if using strain echocardiography would have impacted their results and, in particular, the association between RV function and mortality. More recently, machine learning systems have been developed to facilitate image acquisition and interpretation (15). A system enabling real-time measurements of LV ejection fraction (LVEF) was recently cleared for medical use (Fig. 1). From a four-chamber apical view, it estimates LVEF in a few seconds, without the need to measure LV dimensions. Whether these machine learning-based systems will effectively help clinicians, in particular trainees, is currently under investigation.

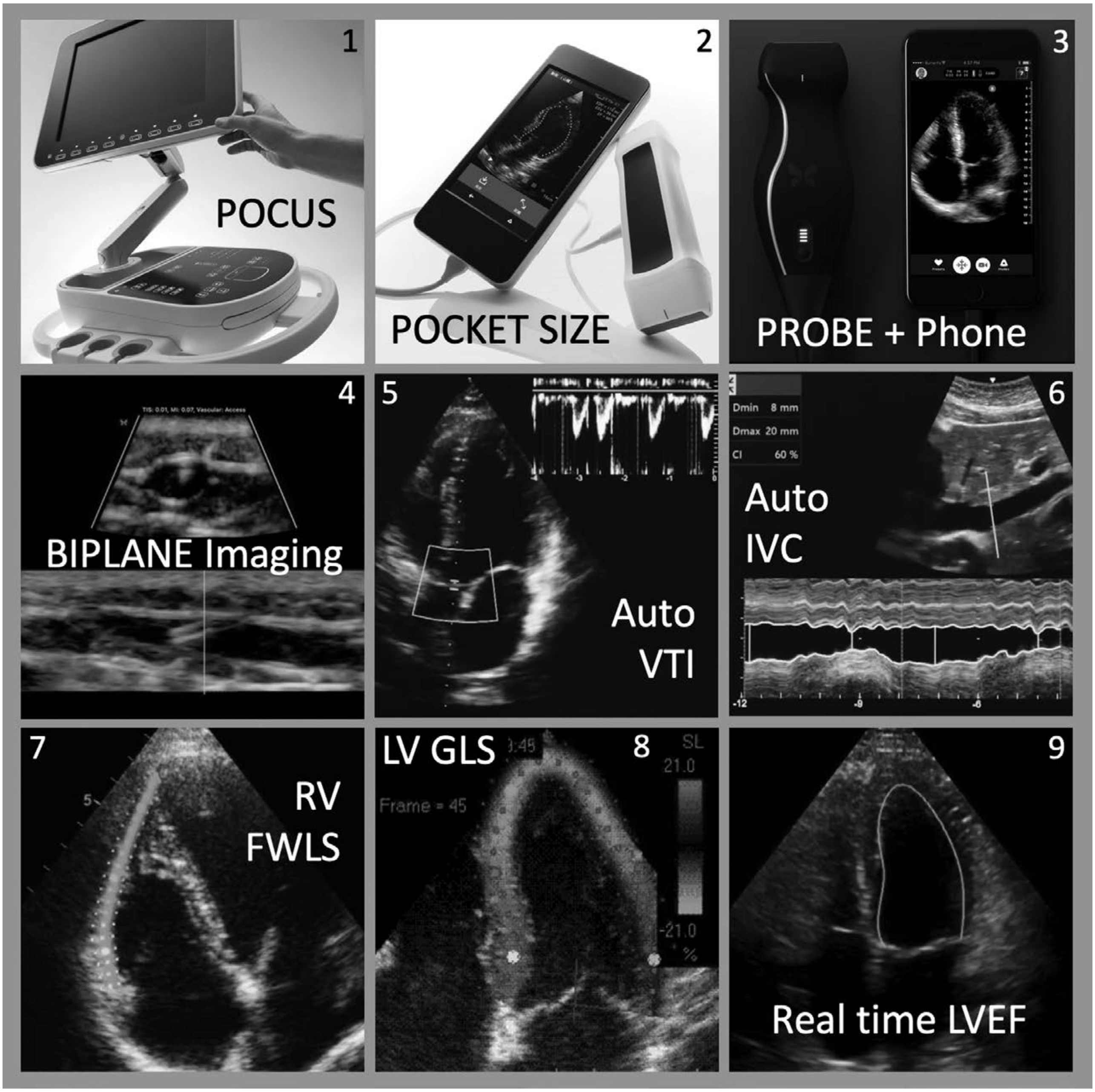

Figure 1. Examples of hardware and software innovations contributing to the rise of point of care ultrasound (POCUS) evaluations in critically ill patients, in particular those with coronavirus disease 2019 (1). Light and easy to move POCUS system used by Chotalia et al (4), from Philips Healthcare (Andover, MA) with permission; (2) pocket size echo-Doppler device, from GE HealthCare (Chicago, IL) with permission; (3 and 4) on-chip digital microbeamforming probe to be connected to a smartphone, enabling the simultaneous visualization of a transversal and longitudinal view to facilitate vascular access, from Butterfly Network (Guilford, CT) with permission; (5 and 6) software enabling the automatic measurement of the subaortic velocity time integral (VTI) and of the inferior vena cava (IVC) diameter respiratory variations; (7 and 8) speckle tracking software enabling the automatic quantification of the right ventricular free wall longitudinal strain (RV FWLS) and of the left ventricular global longitudinal strain (LV GLS) which are markers of myocardium shortening; (9) machine learning-enabled real-time measurement of left ventricular ejection fraction (LVEF), from GE Healthcare with permission.

OTHER HEMODYNAMIC MONITORING METHODS

In the above-mentioned international survey (12) on the hemodynamic monitoring and management of COVID-19 ICU patients, transpulmonary thermodilution, pulse contour methods, and pulmonary thermodilution were used to assess cardiac output by 43%, 29% and 13% of respondents, respectively.

Transpulmonary thermodilution enables an estimation of extravascular lung water, which may help manage patients with pulmonary edema. However, it does not discriminate between RV and LV function and requires the use of a femoral arterial catheter. Pulse contour methods are minimally invasive and easy to setup. They provide beat-to-beat measurements of stroke volume, which is useful when performing preload-modifying maneuvers to detect fluid responsiveness. Unfortunately, most pulse contour algorithms are influenced by systemic vascular resistance and are therefore not recommended for the hemodynamic assessment of septic patients. The pulmonary artery catheter enables the assessment of pulmonary artery pressures and mixed venous oxygen saturation, which may be useful in patients with pulmonary hypertension and intrapulmonary shunt. Specific catheters may even give an estimate of RV end-diastolic volume and ejection fraction. Unfortunately, tricuspid regurgitation, a well-known limitation of pulmonary thermodilution techniques, is frequent and more significant in case of RV dilation. Finally, the large randomized controlled trial that investigated the outcome impact of pulmonary artery catheter in patients with ARDS did not report any clinical benefits (16).

In summary, COVID-19 ICU patients are frequently hemodynamically unstable. Echocardiographic phenotypes vary from hyperkinetic states to low-flow states related to hypovolemia, LV, and RV dysfunction. As illustrated by Chotalia et al (4), RV dysfunction is frequent in mechanically ventilated patients with ARDS, and the combination of RV dilation and systolic dysfunction is associated with mortality. These findings suggest that an echocardiography should be performed without delay in all COVID-19 patients with hemodynamic instability. Luckily, the miniaturization of ultrasound devices, recent software innovations, and the plethora of training programs facilitate the adoption of POCUS evaluations by intensivists.

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REFERENCES

1. Michard F, Vieillard-Baron A: Critically ill patients with COVID-19: Are they hemodynamically unstable and do we know why? *Intensive Care Med* 2021; 47:254–255
2. Szekely Y, Lichter Y, Taieb P, et al: Spectrum of cardiac manifestations in COVID-19: A systematic echocardiographic study. *Circulation* 2020; 142:342–353
3. Dweck MR, Bularga A, Hahn RT, et al: Global evaluation of echocardiography in patients with COVID-19. *Eur Heart J Cardiovasc Imaging* 2020; 21:949–958
4. Chotalia M, Ali M, Alderman JE, et al: Right Ventricular Dysfunction and Its Association With Mortality in Coronavirus Disease 2019 Acute Respiratory Distress Syndrome. *Crit Care Med* 2021; 49:1757–1768
5. Vieillard-Baron A, Schmitt JM, Augarde R, et al: Acute cor pulmonale in acute respiratory distress syndrome submitted to protective ventilation: Incidence, clinical implications, and prognosis. *Crit Care Med* 2001; 29:1551–1555
6. Mekontso Dessap A, Boissier F, Charron C, et al: Acute cor pulmonale during protective ventilation for acute respiratory distress syndrome: Prevalence, predictors, and clinical impact. *Intensive Care Med* 2016; 42:862–870
7. Lassen MCH, Skaarup KG, Lind JN, et al: Echocardiographic abnormalities and predictors of mortality in hospitalized COVID-19 patients: The ECHOVID-19 study. *ESC Heart Fail* 2020; 7:4189–4197
8. Baycan OF, Barman HA, Atici A, et al: Evaluation of biventricular function in patients with COVID-19 using speckle tracking echocardiography. *Int J Cardiovasc Imaging* 2021; 37:135–144
9. Schneider M, Aschauer S, Mascherbauer J, et al: Echocardiographic assessment of right ventricular function: Current clinical practice. *Int J Cardiovasc Imaging* 2019; 35:49–56
10. Vieillard-Baron A, Prigent A, Repessé X, et al: Right ventricular failure in septic shock: Characterization, incidence and impact on fluid responsiveness. *Crit Care* 2020; 24:630
11. Gonzalez F, Gomes R, Bacariza J, et al: Could strain echocardiography help to assess systolic function in critically ill COVID-19 patients. *J Clin Monit Comput* 2021 Feb 27. [online ahead of print]
12. Michard F, Malbrain ML, Martin GS, et al: Haemodynamic monitoring and management in COVID-19 intensive care patients: An international survey. *Anaesth Crit Care Pain Med* 2020; 39:563–569
13. Vieillard-Baron A, Millington SJ, Sanfilippo F, et al: A decade of progress in critical care echocardiography: A narrative review. *Intensive Care Med* 2019; 45:770–788
14. Morris DA, Krisper M, Nakatani S, et al: Normal range and usefulness of right ventricular systolic strain to detect subtle right ventricular systolic abnormalities in patients with heart failure: A multicentre study. *Eur Heart J Cardiovasc Imaging* 2017; 18:212–223
15. Asch FM, Poilvert N, Abraham T, et al: Automated echocardiographic quantification of left ventricular ejection fraction without volume measurements using a machine learning algorithm mimicking a human expert. *Circ Cardiovasc Imaging* 2019; 12:e009303
16. Wheeler AP, Bernard G, Thompson BT, et al: Pulmonary artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med* 2006; 354:2213–2224