Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The disproportionate inflammatory response to SARS-CoV-2 is likely the cause of death of several COVID-19 patients as a result of acute respiratory distress syndrome and initial immunothrombosis. Corticosteroids and other immune suppressant agents might be used, with particular attention to the timing of administration. At the moment, steroids are used extensively to prevent this excessive inflammatory response, but they have proven to be ineffective or even dangerous when administered during the early phases of the disease[3] or to young patients.[4]

Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome[5] can worsen hypoxia and cause death in a large proportion of patients. This syndrome consists of in situ pulmonary clot formation but does not exclude the classic thromboembolism. For this reason, thromboprophylaxis is an essential element for a favorable prognosis, and full anticoagulation is a mainstay of advanced treatment.

Complications of preexistent comorbidities or ongoing therapies (multidrug-resistant bacterial pneumonia or severe immune suppression) are other important, indirect causes of COVID-19 patients' deaths, together with rare acute clinical manifestations (eg, myocarditis).

In Italy, we estimate that patients dying in the ICU accounted for only 18% of the total number of deaths. The mean length of ICU stay was 15 days, with a 50% mortality rate[6] (529,946 bed-days were registered from February 21, 2020–February 21, 2021).[7] The number of ICU deaths was, therefore, 17,664 of 95,992 total,[8] equal to 18%. All other deaths have occurred at home, in healthcare facilities, or in hospital wards, according to each patient's characteristics.

These observations can help readers to interpret the numbers and figures daily distributed by the media.

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Marilena Marmiere, MD*
Filippo D'Amico, MD*
Alberto Zangrillo, MD*,†
Giovanni Landoni, MD*,†

*Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute
†Faculty of Medicine, Vita-Salute San Raffaele University, Milan, Italy

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A Call for Pragmatic Bedside Assessment of Right Ventricular (RV) Function in Coronavirus Disease 2019 (COVID-19)

To the Editor:

We read with interest Isgro et al.'s[1] recent article, describing the potential for right ventricular dysfunction (RVD) in critically ill patients with coronavirus disease 2019 (COVID-19). We agree that the combination of micro/macro thrombi, myocardial injury, sepsis with a profound systemic inflammatory response, along with the combination of Acute Respiratory Distress Syndrome and injurious invasive ventilation, are likely to reflect a *perfect storm* of pathophysiology in which right ventricular (RV) dysfunction is highly likely to occur.

The authors suggest that RVD is present when echocardiography parameters (including RV fractional area change, tricuspid annular plane systolic excursion and pulsed-Doppler S'Wave velocity) are "less than the lower value of the normal range." While we wholeheartedly support the use of echocardiography as the cornerstone technique for assessment of RV function in this patient group, we call for a pragmatic approach that includes the combination of both qualitative and quantitative parameters.[2]

The quantitative parameters described by the author have not yet been validated in this population, either to a clinical endpoint or against a reference method. In other settings, they have been shown to be inconsistent for prediction of poor RV function when compared with reference methods, and perhaps more challengingly, have been observed to vary in their predictive performance depending on the degree of RVD present.[3]

Indeed, in the prospective study of 100 consecutive patients with COVID-19 presenting to the hospital by Szekely et al., even in the most critically ill cohort (those receiving invasive mechanical ventilation, n = ten), mean ± standard deviation values for pulsed Doppler S'Wave velocity and tricuspid annular plane systolic excursion were within the normal range (10.1 ± 3cm/s and 2.1±cm, respectively)[4]. Yet, in this cohort, RV dilatation (as measured by RVEDA) right ventricular end diastolic area was a common abnormality. Where quantitative parameters are used, their combination may allow better discrimination of normal and abnormal RV function.[5]

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Two-dimensional speckle-tracked RV longitudinal strain has been suggested as a method to overcome some of the difficulties associated with the conventional quantitative parameters and, although showing promise in research settings, has not yet found widespread use in clinical practice.

During the pandemic, critical care echocardiography, delivered by clinicians at the bedside, has been essential for the management of critically ill patients with COVID-19. In such a setting, focused intensive care echocardiography often does not include the ability to measure quantitative parameters and is reliant on answering qualitative questions; *is the RV dilated or not?*[6] *Is there RV dysfunction or not*? We have heard anecdotal reports of quantitative echocardiography (such as that offered by an accredited echocardiography service) not being available in "red-zone" (COVID) intensive care units due to concerns regarding staff safety.

We agree with Isgro et al. that there is a need for large-scale prospective echocardiography data in COVID-19 patients. To this end we are conducting a multicenter prospective transthoracic echocardiographic study, to explore the incidence of RV dysfunction in critically ill patients ventilated with COVID-19 (COVID-RV), which currently is recruiting in 12 Scottish intensive care units.[7] Given the difficulties in RV assessment described, the presence of RVD for this study includes the qualitative parameters of RV dilatation, interventricular septal flattening, and a *subjective* description of "dysfunction." These measures previously have been demonstrated to be associated without outcome in patients with acute respiratory distress syndrome.[8,9] The use of quantitative parameters, including speckle- racked longitudinal strain, will be explored off-line as secondary outcomes and will help provide further mechanistic insights.

Isgro et al. highlighted the need for prospective studies of RV protection in patients with COVID-19. We applaud this aim, and like them, we believe such an approach could lead to meaningful patient benefit. We urge, however, that any research forming such a study, or indeed when describing appropriate inclusion criteria for a trial, should include an echocardiographic definition of RVD that is sufficiently pragmatic to empower the bedside clinician to make the diagnosis.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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Philip McCall, MBChB, FRCA, AFICM, MD[*,†,1]
Jennifer Mary Willder, MBChB, BSc (Hons), FRCA, PhD[‡]
James McErlane, MBBS, MA, MSc, MRCP[§]
Ben Shelley, MBChB, FRCA, DipPaed, FFICM, MD[*,†]
[*]*University of Glasgow, Glasgow, UK*
[†]*Golden Jubilee National Hospital, Glasgow, UK*
[‡]*West of Scotland School of Anaesthesia, NHS Education for Scotland, Glasgow, UK*
[§]*South Eastern Health and Social Care Trust, Northern Ireland, UK*

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Neurologic Injury in Patients With COVID-19 Who Receive VV-ECMO Therapy: A Cohort Study

To the Editor:

THROMBOTIC AND BLEEDING events have been implicated in the progression of coronavirus disease 2019 (COVID-19).[1,2] This dysregulation of coagulation has been associated with poor prognoses.[3,4] Neurologic sequelae, such as ischemic stroke and intracranial hemorrhage (ICH), have been reported in patients with COVID-19 at rates of 0.9%-to-2.3% and 0.9%, respectively.[5,6,7,8] Limited data exist on neurologic events in patients with COVID-19 in the intensive care unit who require extracorporeal membrane oxygenation (ECMO) due to severe acute respiratory distress syndrome (ARDS).

We retrospectively reviewed adult patients with COVID-19 supported by ECMO at our tertiary care center. Inclusion criteria were (1) a positive polymerase chain reaction (PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and (2) cannulation for venovenous (VV) ECMO support. Patient demographics, past medical history, adverse events during hospitalization, laboratory values on day one of ECMO, ECMO variables, and outcomes were obtained through electronic medical records. Neurologic events, such as ischemic stroke, hypoxic ischemic brain injury, ICH, and cerebral microbleed (CMB), were identified based on computed