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EDITORIAL

Haemodynamic response to COVID-19 and its outcome implications

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This editorial refers to 'Risk prediction in patients with COVID-19 based on haemodynamic assessment of left and right ventricular function' by P. Taieb *et al.*, pp. 1241–54.

COVID-19, the syndrome caused by the severe acute respiratory syndrome coronavirus 2, has dominated the global medical landscape for the past 2 years. The clinical picture and outcomes have been fairly well characterized, and vaccination proven to prevent the development of infection and attenuate the severity of its manifestations. While the majority of individuals infected with COVID-19 will experience only a mild, influenza-like illness and recover uneventfully, the requirement for hospitalization portends a much worse outcome. Hospitalized COVID-19 patients with (pre-existing) cardiac disease have a high rate of thrombo-embolism, septic shock, and death.[1] Despite large numbers of individuals having been hospitalized and their cardiovascular systems supported artificially, the haemodynamic profile of the disease has not been adequately characterized. Furthermore, the prognostic implications of various haemodynamic patient subsets have not been comprehensively described.

In the current issue of the journal, Taieb *et al.*[2] investigated the non-invasive haemodynamic profile of 531 hospitalized patients with COVID-19. Reassuringly, 44% of these patients had normal left ventricular and right ventricular haemodynamics. Bilateral ventricular function was stratified into four groups: (i) normal filling pressure and normal output, (ii) normal filling pressure and low output, (iii) high filling pressure and normal output, and (iv) high filling pressure with low output. While abnormal right ventricular haemodynamics correlated with clinical status, it was not associated with worse outcome. Perturbation of left ventricular haemodynamics (stroke volume index, E/e′, and stroke work index), however, was associated with worse outcome. The non-invasively defined haemodynamic profile (four abovementioned groups) of COVID-19 patients was independently associated with mortality and demonstrated incremental value beyond a well-recognized clinical risk score [the Modified Early Warning Score (MEWS)].

Few data have been published on the non-invasive haemodynamic profile of COVID-19 patients. In a study of 23 individuals infected with COVID-19, non-invasively measured haemodynamics revealed a high cardiac index and a low systemic vascular resistance index, similar to what would typically characterize a hyperdynamic state.[3] A variety of underlying mechanisms were proposed, including hypoxaemia, viral sepsis, and peripheral shunting.[3] The near-normal PaO_2 found in the majority of patients in this study suggests that hypoxaemia was not the primary driver for the hyperdynamic circulatory response.[3] Evidence for hepatic arteriovenous shunting is indirect and originates from portal vein dilatation seen in autopsy studies.[3,4] Viral sepsis secondary to COVID-19 infection with direct vasodilatory effects is an attractive theory to explain most of the haemodynamic observations, but unfortunately is not a well-defined entity.[3,5] Interestingly, despite pulmonary involvement being the common denominator of COVID-19 infection, in the series described by Busana *et al.*,[3] pulmonary pressures and the total pulmonary resistance were not elevated. This unexpected observation may have been caused by pulmonary capillary recruitment or intrapulmonary neoangiogenesis.[3,6] In a series of 21 mechanically ventilated COVID-19 patients, invasive measurements revealed a haemodynamic profile similar to the patients described by Busana *et al.*, although comparison with the current study is made challenging due to the very different risk profile of the study population.[7]

The haemodynamic profile of COVID-19 patients in the study of Busana *et al.* contrasts sharply with a large number of those in the current analysis,[2] where the indexed stroke volume was impaired in 46% of patients, high systemic vascular resistance was observed in 61% and pulmonary hypertension in 76%.[2] These conflicting data may be reconciled by the fact that Busana *et al.*[3] described the haemodynamic profile of COVID-19 early during the course of the disease (mean of 8.9 ± 6.6 days after symptom onset), while time to symptom onset is not mentioned by Taieb *et al.* Patients included in the current analysis may have been more severely ill: 44% required supplemental oxygen administration and/or non-invasive ventilation, while mechanical cardiorespiratory support or the institution of

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vasopressors[2] was mandated in 4%. In contrast, while the number of patients in the study by Busana *et al.*[3] who required supplemental oxygen or non-invasive support was not reported, no patients required mechanical respiratory or inotropic/vasopressor support. The administration of vasopressors and/or sympathetic activation by dyspnoea and assisted ventilation may account for at least some of the elevated systemic vascular resistance documented by Taieb *et al.*[2] The discrepancies between these two studies clearly demonstrate that more data are needed on the haemodynamic profile of COVID-19 infection, and especially on its temporal course and evolution over time.

The non-invasive characterization of the haemodynamic profile of hospitalized COVID-19 patients has obvious advantages compared to invasive monitoring when taking into account the large disease burden and the required infection prevention measures. While the current study does not contain any validation of non-invasive haemodynamic parameters in the specific COVID-19 patient subset, comparisons between the invasive and non-invasive haemodynamic descriptors employed have been published for non-COVID populations. The meticulous data collection on the haemodynamic profile of a large population of hospitalized COVID-19 patients in the current study has provided evidence that may be useful for clinical risk stratification.[2] How long the COVID-19 pandemic will last is open to debate, and whether the classification system proposed will prove to be useful in planning patient management is still unknown. The data collected by Taieb *et al.*,[2] however, while relevant for the duration of the COVID-19 pandemic, might remain applicable in the future, since the COVID-19 virus and its clinical picture have many features in common with other viral respiratory diseases.

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