Hypotension, Systemic Inflammatory Response Syndrome, and COVID-19: A Clinical Conundrum

To the Editor

Clinicians who have treated large number of critically ill patients with coronavirus disease 2019 (COVID-19) would generally agree on several core observations: (1) intensive care unit (ICU) admissions for COVID-19 patients occurred almost exclusively for worsening respiratory failure; (2) doses of sedatives and analgesics to facilitate mechanical ventilation in COVID-19 patients were substantially elevated when compared with critically ill patients without COVID-19; and (3) systemic hemodynamics of most COVID-19 patients, including those with acute respiratory distress syndrome (ARDS), were remarkably preserved, unless heart failure, an acute thrombotic event, or superimposed bacterial sepsis complicated the disease.

The first clinical description of ICU admissions for COVID-19 in the United States concluded that “most patients did not present with evidence of shock.” This is supported by a larger study from ICUs in New York City area where median lactate value of 223 studied critically ill patients was 1.5 mmol/L. Isolated cases of COVID-19–induced shock continue to be discussed as case reports.

Hence, the most typical clinical picture of a critically ill patient with COVID-19 that one encounters in the ICU is a patient who is deeply sedated and sometimes paralyzed, has a severely impaired alveolar gas exchange, and requires none or relatively low doses of intravenous vasopressors (eg, norepinephrine at rates typically lower than 5 µg/min). These mild degrees of hypotension can often be attributed to high doses of sedatives, positive pressure ventilation with high levels of positive end-expiratory pressure (PEEP), restrictive fluid management, and aggressive diuresis. In the absence of elevated lactate, these physiologic characteristics do not fulfill criteria for shock. In our experience, many patients in fact required resumption of their home antihypertensives while being mechanically ventilated.

These observations of preserved hemodynamics and the absence of shock in a syndrome that has been characterized by “cytokine storm” with markedly elevated levels of certain interferons, interleukins, and chemokines are curious and stand in contrast to other cohorts of critically ill patients with ARDS who commonly present with distributive shock and require fluid resuscitation and higher levels of hemodynamic support.

Due to significant increases in plasma levels of interleukin (IL)-6 in COVID-19, similarities have recently been drawn to cytokine release syndrome and acute lung injury that sometimes occur after chimeric antigen receptor (CAR) T-cell therapy. Consequently, trials targeting IL-6 are ongoing in patients with COVID-19. Having managed patients after CAR T-cell infusions ourselves, we must question these proposed similarities between COVID-19 disease and CAR T-cell therapy—CAR T-cell patients with cytokine release syndrome often require large amounts of fluid resuscitation due to capillary leak, resulting in pulmonary or even airway edema, and hypotension is often present even in milder cases of cytokine release resulting in the need for vasopressor support in the ICU.

With these observations and data as a backdrop, one now needs to reconcile the following: we have historically attributed the hypotension of ICU patients with sepsis and ARDS to the “systemic inflammatory response syndrome (SIRS)” after ensuring that patients are euvoletic and their cardiac function is adequate. We have believed that SIRS drives vasodilation, capillary leak, and hypotension. Critically ill COVID-19 patients with ARDS who commonly present with ARDS who commonly present with cytokine release syndrome often require large amounts of fluid resuscitation due to capillary leak, resulting in pulmonary or even airway edema, and hypotension is often present even in milder cases of cytokine release resulting in the need for vasopressor support in the ICU.

While COVID-19–related ARDS has been proposed to be a “unique type of ARDS” (due to extensive microcapillary thrombosis, pulmonary angiogenesis, preserved respiratory system compliance in a subset of patients), it is also important to investigate why this hyperinflammatory syndrome is accompanied by a remarkably preserved hemodynamic picture. Clearly not all severe systemic inflammatory responses are equal.

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DOI: 10.1213/ANE.0000000000005061

Funding: D.H. is supported by a Clinical Investigator Award from the National Heart, Lung and Blood Institute (K08HL141694).

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COVID-19: Epidemiological Factors During Aerosol-Generating Medical Procedures

To the Editor

We read with great interest the important editorial by Orser1 that outlines recommendations for performing aerosol-generating medical procedures (AGMPs). The coronavirus disease 2019 (COVID-19) pandemic places health care workers (HCWs) at high risk of exposure. As of April 2020, HCWs comprised 10% of the COVID-19 cases in Italy.2 We agree that extreme caution must be exercised and preventative strategies be used when performing AGMPs, including tracheal intubation and manual ventilation, to minimize the risk of transmission.1,3

This article broadens the current COVID-19 infectious control strategies through the concept of the epidemiological triad to further protect HCWs performing AGMPs.

John Snow,4 a pioneer anesthesiologist and father of modern epidemiology, first described the epidemiologic triad to trace the source of cholera outbreaks in London in the 1850s. The epidemiological triad (Figure) helps us understand the spread of diseases through 3 components: agent, environment, and host.4 In the context of COVID-19, the agent is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), including the pathogenicity and virulence of various strains. The environment refers to extrinsic factors that affect the agent and opportunities for exposure like respiratory droplets and contaminated surfaces. The host is any uninfected person and their individual susceptibility characteristics (eg, age, sex, and comorbidities). Minimizing the interactions between these components would reduce the spread of COVID-19.

Factors that disrupt the proliferation of COVID-19 can be conceptualized into 3 scenarios (Figure): community, hospital, and AGMPs. “Interrupting factors” (IFs) between any 2 components can be categorized as agent–host IFs (decreasing the host’s susceptibility or diminishing the virus’ virulence), agent–environment IFs (eliminating or decreasing the viral burden in droplets and surfaces), and environment–host IFs (decreasing the opportunity for active virus to infect new hosts).

AGENT–HOST IFs

While a COVID-19 vaccine and/or treatment is the most effective agent–host IFs, they are still being developed. Thus, the focus should remain on promoting practical strategies that optimize environment–host and agent–environment IFs until a vaccine or treatment becomes available.

ENVIRONMENT–HOST IFs

Environment–host IFs in the community include shelter–in–place policies and social distancing. Similarly, hospitals have implemented interim cancellations of elective surgical cases, restricted hospital visitors, and encouraged personal protective equipment (PPE) use. In both settings, frequent hand washing or disinfection, avoidance of physical contact, and restraint from touching one’s face have been vital to controlling the spread of COVID-19.3

During AGMPs, PPE (including N95 respirators, powered air purifying respirators [PAPRs], face shields, gowns, and gloves) remains the major environment–host IF protecting HCWs. For AGMPs, such as intubation, video laryngoscopy provides slightly more distance between the infected patient and the HCW when compared to direct laryngoscopy, but the HCW still remains at high exposure risk. Although various innovative plastic barrier enclosure devices for performing AGMPs have been widely publicized,3 these barriers remain an exposure risk when removed or cleaned as the virus is temporarily contained rather than eliminated. Following the AGMP, HCWs must also remain cautious of exposed areas within the barrier, including the patient’s head, operating room (OR) table, and the HCW’s own clothing, as infectious particles may settle on these surfaces.

AGENT–ENVIRONMENT IFs

Agent–environment IFs in the community include the self–quarantine of infected individuals, respiratory hygiene, mask wearing by infected individuals, and restriction of travel from areas with widespread ongoing transmission. In hospitals, airborne infection isolation rooms (AIIRs or negative pressure rooms) and dedicated hospital wards with devoted COVID health care teams limit transmission to the rest of the hospital. Despite these isolation measures, extensive contamination of environmental surfaces is found in the rooms of COVID-19 patients.3 Because

DOI: 10.1213/ANE.000000000005962