

## Care for Critically Ill Patients With COVID-19

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**Initial reports** suggest that COVID-19 is associated with severe disease that requires intensive care in approximately 5% of proven infections.<sup>1</sup> Given how common the disease is becoming, as in prior major severe acute respiratory infection outbreaks—SARS (severe acute respiratory syndrome), MERS (Middle East respiratory syndrome), avian influenza A(H7N9), and influenza A(H1N1)pdm09—critical care will be an integral component of the global response to this emerging infection.

The rapid increase in the number of cases of COVID-19 in Wuhan, China, in late 2019 highlighted how quickly health systems can be challenged to provide adequate care.<sup>1</sup> Case-fatality proportions were 7-fold higher for patients in Hubei Province compared with those outside of the region, 2.9% vs 0.4%, emphasizing the importance of health system capacity in the care of patients who are critically ill with COVID-19.<sup>1</sup>

This article discusses issues pertaining to regions where critical care units have the capacity to provide mechanical ventilation, acknowledging that this capacity does not exist in many regions and that capacity could be exceeded in many places. This differential ability to manage the disease will likely have a substantial influence on patient outcomes.

### Factors Associated With Requiring Intensive Care

Appreciating typical clinical features and disease course are crucial both to prepare for increasing numbers of patients and to determine how to best treat infected persons. Patients who have required critical care have tended to be older (median age ~60 years), and 40% have had comorbid conditions, commonly diabetes and cardiac disease.<sup>2</sup> Children generally have been observed to experience a milder illness, although perinatal exposure may be associated with substantial risk. The small numbers of pregnant women infected thus far have had a mild course,<sup>3</sup> but limited cases make predictions about disease course uncertain; however, severe illness in pregnant women was a major concern with influenza A(H1N1)pdm2009. The median duration between onset of symptoms and ICU admission has been 9 to 10 days, suggesting a gradual deterioration in the majority of cases.<sup>4</sup> The most documented reason for requiring intensive care has been respiratory support, of which two-thirds of patients have met criteria for acute respiratory distress syndrome (ARDS).<sup>2</sup>

### Differentiating From Other Diseases

Given the presence of a number of circulating respiratory viruses, differentiating COVID-19 from other pathogens, particularly influenza, is important and chiefly done using upper (nasopharyngeal) or lower (induced sputum, endotracheal aspirates, bronchoalveolar lavage) respiratory tract samples for reverse transcriptase–polymerase chain reaction and bacterial cultures. There are suggestive but nonspecific radiographic changes, such as ground-glass opacities on computed tomography.<sup>2</sup> Rapid access to diagnostic testing results is a public health and clinical priority, allowing for efficient patient triage and implementation of infection control practices.

### Clinical Management and Outcomes

Management of severe COVID-19 is not different from management of most viral pneumonia causing respiratory failure (Figure). The principal feature of patients with severe disease is the development

Figure. Summary of Caring for Critically Ill Patients With COVID-19

Caring for critically ill patients with COVID-19 is based on the usual management of viral pneumonia with respiratory failure with additional precautions to reduce risk of transmission.

#### Usual critical care

Many patients with severe COVID-19 develop acute respiratory distress syndrome (ARDS). Evidence-based guidelines for ARDS in the context of COVID-19 include treatments such as

- Conservative intravenous fluid strategies
- Empirical early antibiotics for possible bacterial pneumonia
- Consideration for early invasive ventilation
- Lung-protective ventilation strategies
- Periodic prone positioning during mechanical ventilation
- Consideration of extracorporeal membrane oxygenation

#### Modifications to usual critical care

- Admission of patients with suspected disease to private rooms when possible
- Use of medical face masks for symptomatic patients during assessment and transfer
- Maintain distancing of at least 2 m between patients
- Caution when using high-flow nasal oxygen or noninvasive ventilation due to risk of dispersion of aerosolized virus in the health care environment with poorly fitting masks
- Clinicians involved with aerosol-generating procedures should use additional airborne precautions including N95 respirators and eye protection

#### Facility planning

- Ensure staff have updated training in infection prevention and control including personal protective equipment
- Planning at local and regional levels for a potential surge in the need for critical care resources

#### COVID-19-specific considerations

Antiviral or immunomodulatory therapies are not yet proven effective for treatment of COVID-19. Patients should be asked to participate in clinical trials of supportive or targeted therapies.

of ARDS: a syndrome characterized by acute onset of hypoxemic respiratory failure with bilateral infiltrates. Evidence-based treatment guidelines for ARDS should be followed, including conservative fluid strategies for patients without shock following initial resuscitation, empirical early antibiotics for suspected bacterial co-infection until a specific diagnosis is made, lung-protective ventilation, prone positioning, and consideration of extracorporeal membrane oxygenation for refractory hypoxemia.<sup>5</sup>

In settings with limited access to invasive ventilation or prior to patients developing severe hypoxemic respiratory failure, there may be a role for high-flow nasal oxygen or noninvasive ventilation.<sup>6</sup> However, the high gas flow of these 2 techniques is less contained than in the closed circuitry typical of invasive ventilators, which poses the risk of dispersion of aerosolized virus in the health care environment, such as in the setting of a poorly fitting face mask. Determining the magnitude of this risk, and mitigation strategies, is a crucial knowledge gap.

Septic shock and specific organ dysfunction such as acute kidney injury appear to occur in a significant proportion of patients with COVID-19-related critical illness and are associated with increasing mortality,

with management recommendations following available evidence-based guidelines.<sup>7</sup>

While no antiviral or immunomodulatory therapies for COVID-19 have yet proven effective, a majority of severely ill patients described to date have received numerous potentially targeted therapies—most commonly neuraminidase inhibitors and corticosteroids—and a minority of patients have been enrolled in clinical trials.

While mortality among all infected patients may be in the range of 0.5% to 4%,<sup>1</sup> among patients who require hospitalization, mortality may be approximately 5% to 15%, and for those who become critically ill, there is currently a wide mortality range, from 22% to 62% in the early Hubei Province case series.<sup>2,4</sup> The exact cause of death is unclear at this point, with progressive hypoxia and multi-organ dysfunction being the presumed causes. Case-fatality proportions, both among all COVID-19 patients and among severely ill patients, will likely become more precise and generalizable with increased surveillance to better clarify the number of individuals infected and as greater numbers of infections occur around the globe.

### Protecting Patients and Health Care Workers

Reducing the risk of nosocomial outbreak amplification through transmission of virus to other patients and health care workers is of critical importance. Maintaining appropriate distancing of at least 2 m between patients with suspected or confirmed to have COVID-19, consideration of use of medical masks for symptomatic patients, and, ideally, admission of patients with suspected disease to private rooms are important considerations. Ensuring hospital staff are well trained in standard, contact, and droplet infection prevention and control precautions, including the use of relevant personal protective equipment, is an imperative. Clinicians involved with aerosol-generating procedures such as endotracheal intubation and diagnostic testing using bronchoscopy should additionally use airborne precautions, including N95 respirators or equivalent face masks and face shields or goggles for eye protection.

### Surge Preparation

If increasing numbers of patients with COVID-19 develop severe illness, plans should be made at local and regional levels for how to best manage the potential surge in the need for critical care re-

sources. Furthermore, if access to lifesaving interventions such as hospital beds, ventilators, extracorporeal membrane oxygenation, or renal replacement therapy is likely to be strained, clear resource allocation policies should be determined by clinicians, policy makers, the general public, and ethicists. These active preparation measures can be organized well before large numbers of infected patients require hospital preparation.

### Major Knowledge Gaps

COVID-19 is a novel disease with an incompletely described clinical course, especially for children and vulnerable populations. Risk factors for severe illness remain uncertain (although older age and comorbidity have emerged as likely important factors), the safety of supportive care strategies such as oxygen by high-flow nasal cannula and noninvasive ventilation are unclear, and the risk of mortality, even among critically ill patients, is uncertain. There are no proven effective specific treatment strategies, and the risk-benefit ratio for commonly used treatments such as corticosteroids is unclear.

It is essential to learn as much as possible through observational studies and clinical trials across a breadth of patient populations and care settings. These should incorporate clear measurements of severity of critical illness so that outcomes can be risk adjusted, and use sufficiently common outcome measures to combine data and validly compare observations across regions.<sup>8</sup> Ideally, clinical trials should be structured to promote maximum learning from around the world, such as through the use of master protocols or adaptive platform designs.<sup>9,10</sup>

### Conclusions

In a very short period, health care systems and society have been severely challenged by yet another emerging virus. Preventing transmission and slowing the rate of new infections are the primary goals; however, the concern of COVID-19 causing critical illness and death is at the core of public anxiety. The critical care community has enormous experience in treating severe acute respiratory infections every year, often from uncertain causes. The foundation for care of severely ill patients with COVID-19 must be grounded in this evidence base and, in parallel, ensure that learning from each patient is maximized to help those who will follow.

#### ARTICLE INFORMATION

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