SPECIAL ARTICLE

# Initial Clinical Impressions of the Critical Care of COVID-19 Patients in Seattle, New York City, and Chicago

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Since the first recognition of a cluster of novel respiratory viral infections in China in late December 2019, intensivists in the United States have watched with growing concern as infections with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus—now named Coronavirus Disease of 2019 (COVID-19)—have spread to hospitals in the United States. Because COVID-19 is extremely transmissible and can progress to a severe form of respiratory failure, the potential to overwhelm available critical care resources is high and critical care management of COVID-19 patients has been thrust into the spotlight. COVID-19 arrived in the United States in January and, as anticipated, has dramatically increased the usage of critical care resources. Three of the hardest-hit cities have been Seattle, New York City, and Chicago with a combined total of over 14,000 cases as of March 23, 2020.

In this special article, we describe initial clinical impressions of critical care of COVID-19 in these areas, with attention to clinical presentation, laboratory values, organ system effects, treatment strategies, and resource management. We highlight clinical observations that align with or differ from already published reports. These impressions represent only the early empiric experience of the authors and are not intended to serve as recommendations or guidelines for practice, but rather as a starting point for intensivists preparing to address COVID-19 when it arrives in their community. (Anesth Analg XXX;XXX:00–00)

Since the first recognition of a cluster of novel respiratory viral infections in China in late December 2019, intensivists in the United States have watched with growing concern as infections with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus—now named Coronavirus Disease of 2019 (COVID-19)—have spread to hospitals in the United States. Two aspects of COVID-19 have placed critical care physicians in the spotlight. The first is its remarkable transmissibility. Because no herd immunity exists to COVID-19, spread throughout a population is extremely rapid, and case counts in a metropolitan area may increase by hundreds or even thousands per day. The second is that unlike influenza virus infection, COVID-19 is marked by a severe hypoxic respiratory failure requiring prolonged, high-intensity supportive care. Such care includes intubation, sedation and mechanical ventilation, advanced therapies for respiratory failure such as pulmonary vasodilators and prone positioning, cardiovascular support, and even experimental antiviral therapy. Such care is unfortunately also a scarce resource and easily overwhelmed. The "flattening the curve" strategy currently pursued by the United States explicitly acknowledges that, if left unchecked, the spread of COVID-19 through a population can occur sufficiently rapidly that critical care resources may not be available to treat all patients who require it.[1]

Documented spread of COVID-19 to Europe occurred in late January 2020.[2] As experience with COVID-19 in the 2 greatest affected nations (China and Italy) has grown,[3,4] a picture of COVID-19 has gradually come into focus. Although patients may transmit infection while asymptomatic,[5] most cases present with flu-like symptoms, including cough, shortness of breath, fever, and myalgias, and an estimated 80% experience only mild disease and recover with no supportive care.[4] In some, lower respiratory symptoms develop approximately 7 days after the onset of symptoms,

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and approximately 1 of 3 of those develop hypoxemic respiratory failure severe enough to require intubation.[6] In patients meeting World Health Organization (WHO) criteria for COVID-19–associated pneumonia and admitted to the intensive care unit (ICU), nearly all had bilateral infiltrates on chest x-ray (CXR) and most required oxygen therapy.[7] Initial attempts to manage patients with noninvasive ventilation have been abandoned due to rapid progression to intubation[7] and risk of nosocomial spread to caregivers and other patients. Although overall case fatality rates are remarkably similar in both China and Italy,[8] published rates vary dramatically when stratified by age, and early fatality rates in the elderly or those with coexisting diseases may range as high as 15%.[9] More recent observations suggest that with widespread testing and more accurate data on incidence, these numbers are decreasing.

Over the next month, amidst rising numbers of cases, ICU admissions, and deaths, intensivists in the United States have been speculating how they will tackle the challenge of COVID-19–associated respiratory failure when widespread COVID-19 presents in their hospital. In addition to published descriptions such as those above, informal descriptions of critical care for COVID-19 patients in China and Italy have circulated among intensivists worldwide. From these informal descriptions, several aspects of severe respiratory failure in COVID-19 patients are atypical. Most patients who require noninvasive ventilation will progress rapidly to intubation, and early intubation is considered safer for providers and equivalent for patients. Unlike classical acute respiratory distress syndrome (ARDS), lung compliance is not severely reduced, and lung-protective ventilation is well tolerated. Hypoxemia is severe and advanced therapies such as pulmonary vasodilators and prone positioning have met with some success. Once instituted, mechanical ventilation may continue for 10–14 days.

The first-known United States case of COVID-19 arrived in Washington State from China on January 15, 2020,[10] and the first case of COVID-19 in New York arrived from Iran on March 1, 2020.[11] Currently, these 2 states have led the nation in total COVID cases, and now between them have more than 14,000 cases and 170 deaths.[12] What follows may best be described as early clinical impressions and management strategies with respect to initial experience with COVID-19–associated respiratory failure in ICUs in the worst affected cities in the United States to date.

As a disclaimer, these observations represent initial clinical impressions of the critical care of COVID-19–associated respiratory failure and should not be interpreted as evidence or a recommendation for treatment but instead as a starting point for intensivists to consider as they prepare to manage severe COVID-19. This outlined briefing will also not address issues related to health care worker protection and nosocomial transmission because these topics have been extensively covered elsewhere.[13] The cumulative patient care experience represented in the ensuing observations exceeds 300 cases, with over 100 requiring intubation and mechanical ventilation.

## Clinical Presentation

Although a classic "fever, malaise, fatigue, cough" presentation has been described in Chinese and Italian accounts,[3,4] the observed spectrum of COVID-19 presentation in the United States has been surprisingly protean. Chest pain, headaches, altered mental status, and gastrointestinal symptoms (including nausea, abdominal pain, vomiting, and diarrhea) have all been observed with initial presentation of COVID-19. Due to the presence of the SARS CoV-2 virus in stool,[14,15] gastrointestinal symptoms may represent a nosocomial infection risk, but disease transmission via stool has not been a prominent clinical entity. Severe renal and hepatic dysfunction that spares the lungs has been observed, as have electrocardiogram (ECG) abnormalities suggestive of myocardial injury. Disease sufficiently severe to require ICU admission skews toward patients >60 years old, and those with medical comorbidities, such as hypertension, diabetes mellitus, or cardiovascular disease. Even generally healthy older patients appear at increased risk for severe disease. Men also seem to be at increased risk for disease progression. Consistent with other United States reports,[16] a trend toward younger patients requiring ICU admission for severe disease has been noted.

Severe respiratory failure seems to occur approximately 1 week after the onset of initial COVID-19 symptoms, and patients may even feel as if initial flu-like symptoms are resolving when shortness of breath worsens. For patients who require intubation, progression is rapid and may occur over 24 hours. To limit nosocomial spread and because few patients recover from noninvasive ventilation alone, intubation is performed when patients meet defined oxygen requirement criteria.

## Laboratory Testing

As described elsewhere,[7] observed white blood cell counts have rarely been elevated in patients admitted to the ICU with COVID-19. While neutrophil counts are typically not elevated, lymphopenia is common. Procalcitonin levels are also relatively low, and thus its level has been considered to track coinfection with conventionally treatable pulmonary pathogens. Empiric community-associated pneumonia treatment has been used in many protocols.

Published reports find 30%–60% sensitivity with rapid nasal swab polymerase chain reaction (PCR) testing.[15,17] In clinical use, false negatives are common, and a significant minority of patients have initially tested negatively but turned positive after several days. Patients strongly suspected as having COVID-19 infection are thus being maintained on enhanced precautions against nosocomial infection and tested again in several days. Because the pulmonary reaction to SARS-CoV-2 infection may involve host inflammation not unlike cytokine storm syndromes,[18] other inflammatory biomarkers may enhance COVID-19 detection or prognostication and are being monitored. C-reactive protein (CRP) levels have been elevated and appear to correlate with the severity of illness. Elevations in ferritin levels are modest but may also assist, as may interleukin (IL-6) levels. As some patients develop a clinical picture consistent with cytokine storm, daily tracking of laboratory values including standard metabolic and hematologic panels, coagulation values including D-dimers and fibrinogen, CRP, lactate dehydrogenase, and ferritin are being used to identify trends.

As in published reports, clinical observations find modestly elevated biomarkers for hepatic injury in patients admitted with COVID-19.[7] Aspartate aminotransferase levels may be high and seem to correlate with disease severity. Bilirubin levels are generally normal, as are alkaline phosphatase levels. Troponin levels are occasionally elevated, and ST elevations have been observed on admission ECGs in COVID-19 patients. Although the etiology is unclear, myocarditis due to severe inflammation has been observed, consistent with published reports.[19] Because of the potential for and severity of cardiac manifestations of COVID-19, B-type natriuretic peptide (BNP) measurement and serial measurement of cardiac function are often tracked daily.

Coagulation abnormalities, including D-dimer elevations, are frequently observed in severe cases of COVID-19, and D-dimer monitoring is performed in some patients. This finding is consistent with recent observations suggesting that abnormalities in coagulation parameters are present in severe COVID-19 disease and predict a worse prognosis.[20,21]

## Radiography

Patchy opacities are almost always present, even in patients on steroids, and markings are almost always bilateral. The severity of opacifications correlates with the severity of disease. Although a characteristic ground-glass opacity appearance on chest computed tomography (CT) scans has also been published,[22] few CT scans are being obtained due to lack of clinical impact and concerns with nosocomial spread via surface contact. Pleural effusions are uncommonly observed.

## End-Organ Involvement

**Cardiovascular.** Although many patients, even with severe pneumonia, are hemodynamically stable, hypotension with normal cardiac function is being encountered and is being treated with low-dose vasopressors to limit fluid administration. Patients with persistently high fevers or who are dehydrated due to nausea and vomiting before ICU admission may need fluid resuscitation. In published reports and current experience, patients with hypertension are at increased risk for severe COVID-19. Although troponin levels are not normally elevated in patients with isolated respiratory failure, concurrent myocardial injury has been observed. And as noted, ST segment elevations consistent with myocarditis have been described.[19] A severe cardiomyopathy that presents when respiratory symptoms are resolving has also been observed clinically and, as in previously published reports, dramatically increases mortality.[23] Cardiomyopathy often presents as severely depressed ejection fraction and a proclivity for unstable arrhythmias, and ICU mortality from COVID-19 is frequently due to refractory bradycardia or pulseless electrical activity.

**Renal.** Early experience suggests that a mild acute kidney injury (AKI) with small creatinine increases may occur with active COVID-19.[3,4] However, considerably more severe AKI and a refractory metabolic acidosis are increasingly observed. Acid-base abnormalities and hyperkalemia are both common, and laboratory testing suggests an acute tubular necrosis mechanism. An oliguric pattern predominates, and the severity of renal insufficiency correlates with the severity of pulmonary symptoms. Hypotension does not seem to be a predisposing factor. AKI may hamper management by limiting the ability to adjust volume status. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been hypothesized to affect COVID-19 susceptibility.[24] Because both NSAIDs and angiotensin-converting enzyme (ACE) inhibitors may also affect AKI progression, their use has been limited in COVID-19 patients.

**Respiratory.** Consistent with previous descriptions,[7] oxygen support is common in COVID patients admitted to the ICU. Hypoxemia appears out of proportion to the clinical presentation, and patients may have oxygen saturations in the 80%–90% range but not be in overt respiratory distress unless they are moved. Both bilevel and continuous positive airway pressure (BiPAP and CPAP) have a high rate of progression to intubation as does high-flow nasal cannula oxygen ($HFNCO_2$). Intubation and mechanical ventilation are thus occurring earlier and are considered effective control for nosocomial spread including to providers. In most cases, lung compliance is only minimally decreased and positive end-expiratory pressure (PEEP) effectively improves gas exchange. Sedation is often needed in the initial period after intubation due to the need for high PEEP and lung-protective ventilation. Secretions can be substantial and thick. Influenza coinfection rates have ranged as high as 25%. Some success with prone positioning has been noted and support with extracorporeal membrane oxygenation has been tried with strict entry criteria excluding patients with diabetes mellitus, hypertension, and abnormal myocardial function. To date, rates of successful extubation in Seattle and New York are low.

## Treatment

Treatment is largely supportive, and treatment protocols are extremely dynamic and evolving as the world searches for a way to treat COVID-19. Antiviral therapies include (among others) remdesivir, lopinavir, and nitazoxanide. Aminoquinolines have generated interest as a prophylactic and/or disease-slowing agent[25] and an ECG to determine QTc interval before initiating hydroxychloroquine therapy and ongoing telemetry may reduce the risk of aminoquinolone-associated cardiac toxicity. Hydroxychloroquine can only be given orally and is thus unavailable to patients with vomiting or gastrointestinal bleeding. Remdesivir is available only via clinical trial and current exclusions include thresholds of aspartate aminotransferase (AST)/alanine transaminase (ALT) elevations, creatinine clearance, and vasopressor requirements. The remdesivir/lopinavir combination may interact with medications such as clopidogrel, tacrolimus, apixaban, and statins. Whether inhaled or intravenous, no consensus on steroid use exists clinically, although published observations cite empiric use in up to 30% of patients.[7] The IL-6 inhibitor tocilizumab is increasingly used for the treatment of cytokine release (storm) syndrome.

## Health Care Worker Protection

Both powered, air-purifying respirators (PAPR) and N95 masks have been used as personal protective equipment (PPE) for health care workers delivering critical care. Both are recommended.[13] A consistent real-world observation is that PAPRs are scarce and N95 masks are being used for the majority of high-risk interactions with patients. In addition to intubation, high-risk procedures include noninvasive ventilation, $HFNCO_2$, and aerosolizing procedures such as transesophageal echocardiogram examinations, endoscopy, extubation, tracheostomy, chest compressions, and nebulizer treatments. Because PPE scarcity is becoming common, providers are working in a resource-constrained environment and frequently reusing equipment. Negative pressure rooms are also prioritized for all high-risk procedures.

## Resource Mobilization

The scale of potential infection and health care system impact in areas with high case volumes is staggering. COVID-19 is rapidly overwhelming hospitals in endemic areas. A top-down strategy using a Hospital Incident Command System or surge style management structures to mobilize hospital resources has been effective. City-wide distribution of critically ill patients has also been used to moderate the impact on any single hospital.

Key material resources include ventilators and PPE. Maintaining accurate inventories and tracking "burn rate" may help administrators model future needs and direct mitigation strategies. Potentially scarce supplies such as face masks and shields are being reused in the setting of pending or actual shortage. Transport ventilators, conversion of noninvasive ventilators to invasive use, repurposing anesthesia machines as long-term ventilators, and using 1 ventilator for 2 COVID-19 patients are strategies currently being considered to address the anticipated surge in ventilated patients.

Early experience suggests that personnel shortages are likely to occur. Nurses, providers, and physicians are being redirected to effectively staff the large influx of COVID-19 patients. Curtailing or canceling all elective procedures helps create a pool of providers. Strategies for replacing infected caregivers include maintaining clinician pools in reserve to prepare for a long period of high-volume critical care operations.

Training physicians outside the usual specialties (eg, training common problem management to nonintensivist physicians so that they can care for critically ill patients under an intensivist's supervision) may expand the capabilities of specialist providers and is being considered. Potential challenges have included the scope of care and liability. Using anesthesia care teams to provide intubation and invasive line placement services helps critical care teams remain focused on other patient management concerns, especially because donning and doffing PPE can be time-consuming. Likewise, repurposing operating room teams with expertise in flipping patients prone has been used to assist ICU teams in gaining expertise.

Because infection of health care personnel is a threat to adequate clinician and other provider coverage, and thus effective delivery of high-intensity critical care, measures to prevent infection are taking priority over routine patient care concerns. Cohorting providers by location (in COVID-19–specific units), task (tracheal intubation and vascular access), and time (rotating teams) are all elements of current response efforts. Nonessential participation in visits into patient rooms (bedside rounds) for routine care such as physical examinations is being minimized with 1 designated person examining the patient.

Remote monitors and video cameras are being used to minimize contact between groups. Care requiring patient contact such as laboratory draws, intubations, indwelling line placement, and physical examinations are being bundled whenever possible. "Do Not

Resuscitate" and "Do Not Intubate" discussions, where appropriate, are occurring early to potentially prevent unintentional or unnecessary intubations. Such discussions have included renal replacement therapy in patients with AKI. Family contact with patients under COVID-19 precautions remains an unresolved issue as full PPE for family consumes both time and resources.

An emerging challenge in resource allocation is the management of patients who undergo perioperative care under a presumption that they are COVID-19 (−) and then become COVID-19 (+). Personnel and resources used in such episodes must then be taken offline for decontamination and quarantine. Currently, routine testing for COVID-19 before such perioperative care is uncommon and likely to have a high false-negative and real false-positive rate. In addition, decisions to extubate may involve resource-level decisions because early extubation to $HFNCO_2$ may free up a ventilator for another patient but increase the risk of nosocomial infection.

## CONCLUSIONS

To reiterate, the above is not intended to be, and should not be interpreted as guidance or recommendations regarding the critical care of patients with severe COVID-19 infection. Rather, they represent clinical impressions and empiric observations from intensivists on the front lines of the COVID-19 pandemic and are likely to change as experience grows. Although the relationship between age, comorbidities, and COVID-19–associated respiratory failure described in early reports has been replicated in our clinical observations,[4] other observations represent new manifestations of the disease. Among these are clinically severe infections in younger patients and a wide diversity of presenting symptoms, including altered mental status, hepatic, myocardial, and kidney injury, and prolonged periods of nausea, vomiting, and diarrhea. These observations suggest that critical care of severe COVID-19 is likely to evolve rapidly, and the tactical management of critical care resources will need to keep pace. The most dynamic focus is likely to be the search for more consistently effective treatments. A therapeutic ability to alter the clinical course of severe COVID-19 infection has the potential to improve critical care management dramatically.

## DISCLOSURES

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