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COVID-19 Critical Illness: A Data-Driven Review

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has posed unprecedented challenges in critical care medicine, including extreme demand for intensive care unit (ICU) resources and rapidly evolving understanding of a novel disease. Up to one-third of hospitalized patients with COVID-19 experience critical illness. The most common form of organ failure in COVID-19 critical illness is acute hypoxemic respiratory failure, which clinically presents as acute respiratory distress syndrome (ARDS) in three-quarters of ICU patients. Noninvasive respiratory support modalities are being used with increasing frequency given their potential to reduce the need for intubation. Determining optimal patient selection for and timing of intubation remains a challenge. Management of mechanically ventilated patients with COVID-19 largely mirrors that of non-COVID-19 ARDS. Organ failure is common and portends a poor prognosis. Mortality rates have improved over the course of the pandemic, likely owing to increasing disease familiarity, data-driven pharmacologics, and improved adherence to evidence-based critical care.

Keywords

COVID-19; critical care; acute respiratory distress syndrome; ARDS; acute hypoxemic respiratory failure; noninvasive respiratory support; mechanical ventilation

INTRODUCTION

As of April 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused over 150 million cases of coronavirus disease 2019 (COVID-19) and over 3 million deaths worldwide (1). The COVID-19 pandemic has been characterized by local surges of

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infection accompanied by tremendous demand for hospital and intensive care unit (ICU) resources. In parallel with these uniquely challenging conditions, knowledge around the treatment of this novel disease has accelerated rapidly. Here we review the literature surrounding the management of critically ill patients with COVID-19.

An estimated one-fifth to one-third of hospitalized patients with COVID-19 experience critical illness, with clinical decompensation at a median of 9 days from symptom onset and 3 days from hospital admission (2-4). Acute hypoxemic respiratory failure (AHRF) is the most common form of organ failure, contributing to over 90% of COVID-19-related deaths in ICU patients (5, 6). Roughly one-quarter of patients with COVID-19 critical illness require noninvasive ventilation (NIV), two-thirds require invasive mechanical ventilation (MV), two-thirds require vasopressor support, and one in six require renal replacement therapy (6).

The combination of rapidly rising community infection rates and hospitalization of high numbers of critically ill COVID-19 patients with prolonged need for acute organ support has led to unprecedented strain on critical care resources. Multiple countries have reported shortages of ICU beds, mechanical ventilators, dialysis equipment, and medications (7). As a result, hospitals have been forced to consider how scarce resources can be allocated, and providers have been redeployed to rapidly adapted "surge ICUs," areas that are often staffed by nonexperts in nontypical locations (7). This context has been further complicated by shortages of commonly used medications and personal protective equipment (PPE), necessitating deviations from pre-existing standard-of-care treatments and care delivery (7). The effects of these adverse conditions have not yet been fully elucidated but clearly have impacted outcomes—hospital mortality correlates closely with community rates of COVID-19 (8). This highly abnormal practice environment must be considered when evaluating the generalizability of research performed over the course of the pandemic.

MANAGEMENT OF RESPIRATORY FAILURE IN NONINTUBATED PATIENTS

Management Goals

Over three-quarters of patients with COVID-19 critical illness are diagnosed with acute respiratory distress syndrome (ARDS) (5, 6). Nearly 90% of patients with ARDS on ICU admission progress to moderate or severe disease within 7 days (5, 9). Management of COVID-19 AHRF and ARDS largely mirrors usual practice (Figure 1). Initial goals include (*a*) supporting oxygenation and ventilation, (*b*) reducing the need for invasive MV when possible, (*c*) triage to intubation when necessary, and (*d*) minimizing infectious transmission risk to healthcare workers (HCWs). Oxygenation goals in COVID-19 do not differ from usual practice (10). Of note, the limited accuracy of pulse oximetry readings may result in occult hypoxemia, particularly in patients of self-identified Black race (11).

Noninvasive Respiratory Support

Driven by concerns regarding the risk of viral aerosolization during noninvasive respiratory support (12), initial recommendations for management of COVID-19 AHRF emphasized early intubation with limited use of high-flow nasal cannula (HFNC) or NIV (4). Although

HCW infection with COVID-19 during provision of clinical care remains a concern, there has been no clear demonstrable link between noninvasive respiratory support and HCW transmission when utilizing appropriate PPE (13, 14). Notably, aerosol dispersion maybe no worse with HFNC than with conventional oxygen therapy and lowest with closed-circuit ventilation and helmet NIV (15). The use of a surgical mask over the mouth and nose of patients on HFNC substantially reduces dispersal of respiratory aerosols (16) and can even increase the partial pressure of oxygen (PaO2) (17).

The use of HFNC and NIV for COVID-19 has become more widespread in the setting of abating fears of viral transmission with appropriate PPE use and increasing concerns over ventilator scarcity and poor outcomes among patients undergoing invasive MV (6, 18, 19). We recommend emphasis on risk-stratified appropriate infectious precautions (see the sidebar titled Infectious Precautions) during aerosol-generating procedures and respiratory support modalities rather than conventional nasal avoidance of such interventions when clinically indicated (20). Current guidelines recommend using airborne precautions for HFNC and NIV given the uncertain potential for viral aerosolization (10, 20).

Pre-pandemic randomized controlled trials (RCTs) examining the use of HFNC and NIV, including continuous positive airway pressure (CPAP) via facemask or helmet, for AHRF and ARDS demonstrated decreased risk of intubation when compared to conventional oxygen therapy (23). Though previously uncommonly used in the United States, helmet CPAP has gained in popularity during the COVID-19 pandemic given the potential benefits of improved patient comfort and decreased viral aerosolization (15). Systematic reviews suggest reduced mortality for patients with AHRF receiving helmet or facemask NIV but not HFNC, though only helmet NIV appears to confer a survival benefit in sensitivity analyses restricted to patients with moderate or severe hypoxemia (PaO2:FiO2 ratio <200) or patients without acute exacerbations of chronic obstructive pulmonary disease (COPD) or congestive heart failure (CHF) (23). While the reduced intubation risk observed with all modalities compared to conventional oxygen appears robust to such sensitivity analyses, survival benefit may be limited to helmet NIV or patients with mild disease or comorbid COPD or CHF exacerbations (23).

A living systematic review ("living" in that it is iteratively updated with the latest evidence as new research findings become available) and several recent observational studies examining HFNC and NIV for COVID-19-related AHRF provide low-certainty evidence suggesting reduced risk of intubation and reduced mortality compared to conventional oxygen therapy, with a survival benefit comparable to that seen with MV (13, 24, 25). Studies comparing HFNC with NIV for COVID-19 are few, though one prospective cohort study found no benefit of one modality over another for pre-ICU AHRF in adjusted analyses (26). One small RCT in ICU patients demonstrated a reduced need for intubation and an increased number of ventilator-free days with helmet CPAP compared to HFNC, though no difference in mortality or number of respiratory support-free days was observed (27). In general, few published studies of noninvasive respiratory support for COVID-19 adequately adjust for confounders. Additional RCTs are needed to confirm findings from this largely observational evidence base, and several are ongoing at the time of this writing (ISRCTN16912075, NCT04344730, NCT04381923, NCT04326075). At present, most international guidelines and societies recommend the use of HFNC for AHRF not responding to conventional oxygen therapy, though the first-line modality of noninvasive respiratory support varies across guidelines (28).

Self-Prone Positioning

Prone positioning is an established intervention shown to improve alveolar recruitment and reduce mortality in mechanically ventilated patients with moderate to severe ARDS (29). Pre-pandemic observational studies of self-prone positioning in awake, spontaneously breathing, nonintubated patients with ARDS reported temporarily improved oxygenation and no apparent harm (30).

Several observational studies and one small pilot RCT have demonstrated improved oxygenation with self-prone positioning for COVID-19 AHRF (31-33). In the few studies that included control comparator arms, association of self-prone positioning with intubation rates and mortality varied, with one study suggesting delayed intubation (32-34). Of note, improved oxygenation does not necessarily correlate with survival (35), and the mortality reduction from prone positioning in mechanically ventilated patients is seen with prolonged periods of proning (> 16 h), a duration that may not be tolerable in awake patients (31). RCTs are needed to better understand the impact of self-prone positioning on patient outcomes, and several trials are ongoing at the time of this writing (NCT04395144, NCT04347941, NCT04350723, NCT04477655, NCT04344587, NCT04424797, NCT04325906). Given the low quality of the published literature, guidelines currently inconsistently recommend self-prone positioning (10, 36).

Intubation Timing

Determining the optimal threshold and timing of intubation in COVID-19 AHRF remains challenging. In addition to concerns over procedure-related viral aerosolization, advocates of early intubation strategies cite a theoretical risk of self-induced lung injury. However, data supporting such a mechanism of lung injury draw from preclinical and animal studies, and the risk to patients remains unknown (37). Given the risk of complications and poor outcomes among mechanically ventilated patients with COVID-19, many have cautioned against aggressive early intubation (18). However, early reports of alarming mortality rates among mechanically ventilated COVID-19 patients were confounded by immortal time bias, as follow-up time was insufficient to observe outcomes in all patients—and thus overestimated the true mortality rate (38). More recent studies report mortality rates consistent with that of non-COVID-19, ARDS (39).

Ultimately, intubation timing should be patient-specific and balance the risks of MV with the risks of delayed intubation. While the use of HFNC or NIV may reduce the need for MV, patients should be monitored closely for further deterioration or lack of improvement. Delayed intubation may increase mortality in ARDS (40) and the risk of emergent intubation. Emergent procedures allow little time for safe donning and doffing of PPE, which is crucial to mitigate the risk of infectious exposure for HCWs (36).

Observational studies comparing early and late intubation with or without noninvasive respiratory support report mixed outcomes, with a recent meta-analysis reporting no difference in mortality (41). It is important to note that intubation criteria were not explicitly defined or uniformly applied in these studies. Because the decision to intubate is based on subjective clinical judgment, patient selection into early or late intubation groups is determined by numerous measured and unmeasured clinical factors. As such, the relationship between intubation timing and outcomes is heavily confounded by treatment indication and severity of illness. It is difficult if not impossible to eliminate confounding by indication even with highly robust retrospective risk adjustment (42).

Absent RCT data, comparative effectiveness observational studies can be strengthened by following target trial design, restricting study cohorts to risk subgroups of interest, applying advanced causal inference methodology, reporting the strength of risk adjustment, and cautiously interpreting results with special attention to bias from residual confounding (42, 43). One target trial–designed propensity-matched prospective cohort study comparing HFNC with early intubation for COVID-19 AHRF reported significantly more ventilator-free days and shorter ICU stays but no difference in mortality with HFNC; however, the small sample size and large effect estimate motivates scrutiny and further study (44). Additional research is needed to better understand the most effective and safe approach to and duration of noninvasive respiratory support as a first line intervention in COVID-19 AHRF. One RCT is ongoing at the time of this writing (NCT04632043). In general, it is reasonable to take a stepwise approach for patients with COVID-19 AHRF, attempting time-limited trials of noninvasive respiratory support with or without self-prone positioning, along with close monitoring of clinical status and escalation to MV without delay when indicated, rather than prolonged reliance on unproven strategies.

MANAGEMENT OF RESPIRATORY FAILURE IN INTUBATED PATIENTS

Management Goals

Without data supporting substantive deviations from evidence-based management of ARDS, management of COVID-19 AHRF should follow established principles of lung-protective ventilation aimed at minimizing volutrauma, barotrauma, and atelectrauma (45). Early reports of small cohorts of patients with severe hypoxemia and high compliance prompted suggestions of unique pathophysiology in COVID-19 distinct from classical ARDS (46). However, comprehensive evaluations of respiratory mechanics in COVID-19 AHRF confirm clinical manifestations and outcomes consistent with non-COVID-19 ARDS and do not support categorization into compliance-based subphenotypes (39).

Ventilator Management

Approximately 70% of critically ill patients with COVID-19 require invasive mechanical ventilation (6). Based on pre-pandemic RCT data, management guidelines for ARDS strongly recommend low tidal volume ventilation (ideally 4–6, up to 8 mL/kg predicted body weight) with low inspiratory pressures (plateau pressure <30 cm H_2O) and higher positive end-expiratory pressure (PEEP) strategies for patients with moderate to severe ARDS (47). Because high driving pressure (the difference between plateau pressure and PEEP) has been shown to correlate with mortality in ARDS, ventilator settings may be titrated to a goal driving pressure of <15 cm H_2O as an adjunct to low tidal volumes, though randomized trials are needed to evaluate the causal impact of this approach on patient outcomes (48).

Prone positioning of mechanically ventilated patients with moderate to severe ARDS has been shown to significantly improve 28-day mortality both in non-COVID-19 and COVID-19 ARDS (29, 49). As with other ARDS etiologies, prone positioning for COVID-19 patients should be initiated early in the disease process (within the first 48 h) (29). Prone positioning is usually maintained for 16–24 h, though recent reports suggest that prolonged proning (median 36–71 h) until oxygen and PEEP requirements decrease below goal thresholds is feasible, safe, and may result in greater improvements in oxygenation, though it may confer an increased risk of skin and soft tissue pressure wounds (50).

Rescue Interventions

Routine use of recruitment maneuvers is not recommended for patients with ARDS as they have shown no mortality benefit (45, 47, 51). Given reports of high rates of pneumothorax and cardiac dysfunction among mechanically ventilated patients with COVID-19 (52, 53), the risks of barotrauma and hemodynamic compromise with recruitment maneuvers should be considered carefully. The most recent trial data demonstrate no clear survival benefit from the routine use of neuromuscular blockade in patients with ARDS, but expert consensus suggests it may be a useful tool to facilitate ventilator synchrony or prone positioning when used in a bolus or time-limited infusion (up to 48 h) (36, 45, 54). The impact of neuromuscular blockade on outcomes for patients with COVID-19 has not been comprehensively studied.

Given early data suggesting that COVID-19 lung injury is in part mediated by pulmonary angiopathy (55), the use of pulmonary vasodilators presents a theoretically attractive rescue intervention to improve perfusion and reduce dead space ventilation. However, while inhaled pulmonary vasodilators including nitric oxide and prostaglandins have been shown to improve oxygenation in non-COVID-19 ARDS, such improvements are temporary and have not been shown to increase ventilator-free days or survival (56, 57). Case series describing pulmonary vasodilator use in COVID-19 ARDS report inconsistent oxygenation improvements of unclear clinical significance (58). While pulmonary vasodilators are reasonable to consider for refractory hypoxemia, improvement in oxygenation with this intervention should not preclude the use of other proven life-saving interventions such as proning when indicated by prevasodilator assessments.

Despite early equipoise, recent meta-analysis indicates that the use of veno-venous extracorporeal membrane oxygenation (V-V ECMO) reduces mortality for severe ARDS, though with a significant risk of major bleeding (59). Outcomes for patients with COVID-19 treated with V-V ECMO appear similar to outcomes in pre-pandemic ARDS studies, with 90-day mortality reported to be around 40% (60). Approximately 6% of critically ill patients with COVID-19 have been treated with ECMO (6). Current guidelines recommend consideration of ECMO as rescue for refractory hypoxemia in COVID-19 ARDS in settings with access to expertise and resources (10, 36).

Ventilator Liberation

Many patients with COVID-19 require prolonged MV (9). Ventilator liberation protocols such as the ABCDEF bundle reduce delirium, duration of MV, risk of post–intensive care syndrome (PICS), and healthcare costs. Pandemic-related operational shifts present unique barriers to implementation of such protocols, so adaptive strategies to optimize ventilator liberation protocol use are essential (61). Spontaneous breathing trials with pressure support ventilation are associated with improved extubation success rates compared to T-piece trials, which carry the additional risk of aerosol generation (62). Routine use of preventive post-extubation respiratory support with either HFNC or NIV can reduce the risk of reintubation, and post-extubation NIV may reduce mortality, particularly for patients with COPD (63). Though post-extubation studies were conducted in non-COVID-19 respiratory failure, it is reasonable to extrapolate these findings to patients with COVID-19 AHRF.

For patients failing to wean from MV or who require reintubation after an extubation attempt, tracheostomy placement can decrease work of breathing, allow reduced sedation, allow early mobilization and reduced physical deconditioning, facilitate secretion management, and improve patient comfort (64). Approximately 9% of mechanically ventilated patients with COVID-19 ARDS undergo tracheostomy (9). Though there are varying recommendations for tracheostomy timing in the literature, balancing exposure risks to HCWs during aerosol-generating tracheostomy placement and complication risks for patients undergoing prolonged MV, multidisciplinary guidance suggests consideration of tracheostomy after 10 days of MV (65).

GENERAL CRITICAL CARE MANAGEMENT

Multiorgan Failure and Shock

Extrapulmonary organ dysfunction frequently accompanies COVID-19 critical illness; one-quarter of critically ill COVID-19 patients have acute cardiac, kidney, or liver injury, shock, and/or a thrombotic event (6, 53). Cardiac manifestations include biventricular cardiomyopathy in up to one-third of patients, as well as myocarditis, ischemia, and arrhythmias (53). Renal dysfunction is common, with one-third of critically ill patients developing acute kidney injury, and one in six requiring renal replacement therapy (6). Delirium is common in severe COVID-19: One in five ICU patients experiences nonsedative-related toxic-metabolic encephalopathy, which is associated with increased hospital length of stay, reduced likelihood of discharge to home, and increased in-hospital mortality (66). Importantly, family visitation, virtual or in-person, is associated with a lower risk of delirium, though family engagement remains challenging in the setting of limited visitation policies (67). Cardiac and neurologic considerations in COVID-19 are outlined in more detail in other reviews (68-70).

While COVID-19 critical illness is predominantly characterized by respiratory failure, two-thirds of ICU patients require vasopressor support, and septic shock contributes to 40% of deaths among critically ill patients with COVID-19 (4-6). Early reports of elevated proinflammatory cytokines in patients with COVID-19 generated considerable interest in the potential pathophysiologic contribution of immune cell hyperactivation, or “cytokine storm.”

However, cytokine elevations are notably substantially lower than those observed in non-COVID-19 sepsis, cytokine release syndrome, and hyperinflammatory ARDS phenotypes (71). Questions remain regarding the pathologic role of the cytokine response in COVID-19, particularly given observed benefits of immunosuppressive therapies in select patients. The inflammatory profile of COVID-19 is discussed in more detail in another review (72).

Coagulopathy and Thrombosis

Severe COVID-19 is commonly associated with coagulopathy characterized by elevated serum D-dimer and an increased risk of both venous and arterial thromboembolism (6, 73). Although the development of venous thromboembolism (VTE) is common in critically ill patients, the rates of both arterial and venous thrombosis appear higher in COVID-19 than in other comparable diseases (74). Patients admitted to the ICU have particularly high rates of thromboembolism despite routine use of VTE prophylaxis—an estimated one-quarter to one-third of critically ill COVID-19 patients will have a thrombotic event (6, 73).

In light of the burden of morbidity posed by thromboembolism in COVID-19, there has been considerable interest in whether higher doses of anticoagulation may reduce the risk of subsequent thromboembolism. However, recently published RCTs investigating empiric increased-dose anticoagulation in critically ill patients with COVID-19 have failed to show any benefit with either intermediate-dose prophylaxis (enoxaparin 1mg/kg/day) or therapeutic-dose anticoagulation (75). An interim review of a multiplatform RCT, including three RCTs across five continents, suggested that routine therapeutic anticoagulation of critically ill patients with COVID-19 may be associated with increased mortality and major bleeding; however, these data have not been published or peer reviewed at the time of this writing. The ICU arm of this trial was paused for futility (76). Though the benefit of prophylactic intermediate and therapeutic dosing is being called into question, there is agreement that patients with COVID-19 admitted to the ICU should at least receive standard prophylactic-dose anticoagulation unless contraindicated (77).

Delirium, Sedation, and Analgesia

Sedation practices for patients with COVID-19 have tended toward deep sedation in order to maintain ventilator synchrony on lung-protective settings, especially with more limited clinician room entry, and to facilitate paralysis and prone positioning (78). Compared to non-COVID-19 patients, patients with COVID-19 requiring MV receive higher doses of hypnotics, spend more time comatose, and experience fewer delirium-free days; notably, deep and prolonged sedation is independently associated with increased in-hospital mortality (79). Increased demand for analgesic, sedative, and paralytic medications along with pandemic-related supply chain disruptions have resulted in intermittent drug shortages. Such shortages have prompted increased use of previously discouraged sedatives like benzodiazepines, which in the pre-pandemic era had been shown to be associated with worse patient outcomes (78, 80).

For patients with COVID-19 ARDS, expert opinion emphasizes adherence to pre-pandemic evidence-based sedation practices, including goals for minimal or no sedation for most patients; analgesia first; preferential use of short-acting sedatives; regular pain, delirium, and sedation monitoring at least twice daily; and daily sedation interruptions (78). Of particular importance to promote wakefulness and comfort, patients' respiratory drive and ventilator settings should be optimized first before turning to sedation to facilitate ventilator synchrony (78).

Pharmacologic Therapies

Although the role of corticosteroids in non-COVID-19 ARDS is less clear, dexamethasone and other corticosteroids represent the backbone of therapy for patients with severe COVID-19. The benefit of dexamethasone was demonstrated in the RECOVERY Collaborative Group's open-label multi-arm RCT (81). The RECOVERY trial demonstrated reduced mortality in patients with COVID-19 who required supplemental oxygen therapy or other respiratory support, most marked in patients with critical illness who required MV (81). This finding was subsequently confirmed in a meta-analysis that demonstrated reduced mortality and length of stay in critically ill patients with COVID-19 who were treated with systemic corticosteroids (82).

Trials of tocilizumab, an interleukin (IL)-6 inhibitor, initially showed conflicting results; yet, administration early in critical illness may confer a mortality benefit for the severely ill and is now part of multiple national treatment guidelines (83-85). Remdesivir may play a limited role in the management of patients with severe COVID-19. However, the benefit of remdesivir—a reduction in the time to clinical improvement—seems to be limited to patients who require low-flow oxygen (86, 87). Critically ill and mechanically ventilated patients with COVID-19 do not appear to derive a clear benefit, and remdesivir does not appear to reduce mortality for patients with any severity of COVID-19 (86, 87). Other immunomodulatory therapies such as convalescent plasma have failed to show benefit in patients with critical COVID-19 despite early promise (88).

CLINICAL OUTCOMES

Prognosis and Mortality

Reported outcomes from critical illness in COVID-19 are highly variable, with mortality rates as high as 92% among mechanically ventilated patients described early in the pandemic (89). With time and experience, we have seen a gradual global decrease in the mortality of patients with COVID-19, likely due to increased familiarity with the disease, the discovery of therapeutic options, better adherence to evidence-based critical care, and reduced strain on hospital systems (8, 89). A recent meta-analysis estimates the case fatality rate for mechanically ventilated patients with COVID-19 to be approximately 45% (89).

A number of risk factors for mortality have been identified in patients who develop critical illness. Older age and male sex have consistently been identified as leading factors associated with a higher risk of progression to critical illness and death (90). Mortality among mechanically ventilated patients over the age of 80 exceeds 84% (89). Pre-existing comorbid conditions are additional important risk factors for critical illness, particularly obesity, diabetes mellitus, cardiac disease, hypertension, pregnancy, poorly controlled asthma, and sickle cell disease (90).

The development of organ failure and critical illness is an important prognostic factor in the hospitalized patient with COVID-19. In a large multinational observational cohort, patients who required invasive MV had an observed mortality of 49.8% compared to 8.2% in patients who did not require organ support. Each additional organ failure was associated with further increases in mortality in patients who were mechanically ventilated. Mortality was 40.8% among patients requiring MV alone and over 70% for patients requiring MV, vasoactive medications, and new renal replacement therapy (91).

Special Populations

Pregnancy represents a risk factor for critical COVID-19 and has substantial implications for management of critical illness. Important physiologic changes occur over the course of pregnancy that may impact the ease of endotracheal intubation, hemodynamics, and respiratory compliance depending on the gestational age. Additionally, the gravid uterus requires adaptations during prone positioning (92). Observational studies of pregnant patients with COVID-19 suggest that severe or critical disease carries excess risk of both maternal and fetal complications (93). Given the importance of considering both maternal and fetal health, a multidisciplinary approach is imperative.

In numerous countries, minority race or ethnicity, health insurance status, and socioeconomic deprivation are associated with increased risk of contracting COVID-19 and subsequent hospitalization (94). In the United States, Black, Latinx, Indigenous, and Pacific Islander populations experience disproportionately higher overall COVID-19 mortality burden relative to White populations. Chronic disease and lower socioeconomic opportunity are important determinants for mortality and explain differences in COVID-19 deaths between minority and nonminority groups (95). Importantly, major differences in exposure risk and access to healthcare services are primary drivers of disparities in clinical outcome (94, 95). The excessive burden of COVID-19 cases and death among minority Americans highlights inequitable socioeconomic contributors produced by long-standing structural, cultural, and interpersonal racism (96).

Postacute Care Outcomes

The clinical course of patients with COVID-19 critical illness is prolonged and highly morbid, with a high burden of complications, prolonged duration of MV and intensive care, and protracted hospital stays (6, 91). A multifaceted and integrated approach to palliative care is critical to high-quality care in the ICU, especially given the many ways in which recent widespread policies restricting family visitation for infection control purposes pose a challenge to patient-centered care (97).

As seen with other etiologies of ARDS, patients recovering from COVID-19 critical illness are likely to suffer from PICS (98), though the full impact of post-COVID PICS on individuals, caregivers, the workforce, and healthcare systems is yet to be established. In addition to PICS, patients recovered from COVID-19 can represent with recrudescent AHRF resembling organizing pneumonia, which may be steroid responsive, or with chronic post-ARDS fibrotic lung disease (99, 100). The natural history of these diseases has not yet been well described. Post-ICU pulmonary complications are covered in more detail in another review (101).

CONCLUSIONS

COVID-19 has given rise to unprecedented challenges for the field of critical care medicine. The next phase of the pandemic will be shaped by adherence to evolving public health measures to decrease community spread, the emergence of new SARS-CoV-2 variants, and the success of vaccination campaigns. The significance of recently identified variants remains to be seen; some appear to be more transmissible or virulent than the wild-type strain (102). Early data suggest that vaccine antibody response immunogenicity may be limited in some immunosuppressed patients, including those with malignancies and solid organ transplants frequently admitted to ICUs, though more data are needed to determine vaccine clinical efficacy in terms of preventing severe COVID-19 disease in these patients (103). Reassuringly, multiple vaccines are highly effective at preventing severe COVID-19 in the general population. Vaccination is expected to minimize rates of critical illness, demand for hospital and ICU resources, and mortality (104).

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Glossary

AHRF

acute hypoxemic respiratory failure

NIV

noninvasive ventilation, including continuous positive airway pressure (CPAP) and bilevel positive pressure (BiPAP) ventilation

PPE

personal protective equipment

ARDS

acute respiratory distress syndrome

HCW

healthcare worker

Noninvasive respiratory support

modalities including high-flow nasal cannula (HFNC) and noninvasive ventilation (NIV)

HFNC

high-flow nasal cannula, usually providing >15 L/min flow rate

Conventional oxygen therapy

includes conventional nasal cannula up to 6 L/min, nonrebreather mask, and venturi mask up to 15 L/min

PaO2:FiO2 ratio

ratio of partial pressure of oxygen to fraction of inspired oxygen

COPD

chronic obstructive pulmonary disease

Self-prone positioning

awake, nonintubated patients position themselves prone for a variable number of continuous hours

ABCDEF bundle

care bundle to facilitate ventilator liberation, including management of analgesia and sedation, delirium, awakening and breathing trials, early mobility, and family engagement

PICS

post–intensive care syndrome, which includes cognitive, physical, and psychological impairments that may persist for months to years after critical illness

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INFECTIOUS PRECAUTIONS

Special precautions can minimize HCW infectious exposures. To avoid viral particle aerosolization, use surgical masks over HFNC, ensure NIV masks are nonvented with good fit and seal, and use closed, filtered circuits for invasive and noninvasive ventilators (16, 20). Perform intubation and extubation in negative-pressure rooms when available, with minimum necessary staff presence (21, 22). Rapid-sequence intubation with video laryngoscopy is recommended; mask ventilation should be avoided, and if necessary, done using a two-hand technique with a viral filter in place (22). Pre-extubation recommendations include oral and tracheal suctioning, administration of antitussive medications, and cessation of positive pressure prior to endotracheal tube removal (21).

When caring for mechanically ventilated patients with COVID-19, HCWs should at minimum don droplet and contact PPE; when resources permit, airborne PPE should be used in case of ventilator disconnect (36). Airborne and contact PPE including eye protection should be used for all aerosol-generating procedures including HFNC, NIV, bronchoscopy, bronchial suctioning, sputum induction, manual ventilation, intubation, extubation, turning patients for prone positioning, cardiopulmonary resuscitation, tracheostomy placement, and administration of nebulized medications (which, if possible, should be avoided in favor of metered dose inhalers) (36). Data on risk stratification of aerosol-generating procedures continue to evolve.

SUMMARY POINTS

1. Surging COVID-19 case volume, overwhelmed bed capacity, staffing strains, intermittent drug shortages, initial PPE supply limitations, fears and realities of HCW exposure and illness, and evolving understanding of the novel SARS-CoV-2 pathogen and available treatments have fueled rapid operational and clinical practice shifts in critical care.
2. Growing experience with COVID-19 and a burgeoning evidence base highlight the familiar problems of critical illness, for which there are a number of sound tools and strategies, yet many unanswered questions.
3. Medical management of COVID-19-associated AHRF and ARDS largely mirrors usual practice for non-COVID-19 patients.
4. Unique considerations in the care of patients with COVID-19 critical illness include special precautions and procedures to minimize viral transmission risk for HCWs, adherence to critical care best practices under adverse conditions, and the importance of concerted efforts to engage patients and families in patient-centered care despite the challenge of visitation limitations.
5. Important knowledge gaps remain in our understanding of SARS-CoV-2 pathophysiology and ways in which care of COVID-19 patients is distinct from other conditions.
6. Future COVID-19 critical care research should focus on the development of additional disease-modifying interventions as well as how, when, and for whom to apply proven strategies.

FUTURE ISSUES

1. Which patient subgroups will benefit from HFNC, mask or helmet NIV, and self-prone positioning? What is the optimal timing and duration of these interventions for severe COVID-19?
2. Which patient subgroups will benefit from early versus late intubation? What is the optimal timing of intubation?
3. Are there patient subgroups for whom empiric therapeutic anticoagulation improves outcomes?
4. Which patients will benefit from immunosuppressive or immunomodulatory therapies?
5. Can we identify or develop antiviral agents effective in the setting of rapidly progressive critical illness?
6. What social inequities do disparities in outcomes for severe COVID-19 reveal? How can disparities be mitigated and prevented in the delivery of critical care?
7. What ICU interventions can improve postacute COVID-19 syndrome?

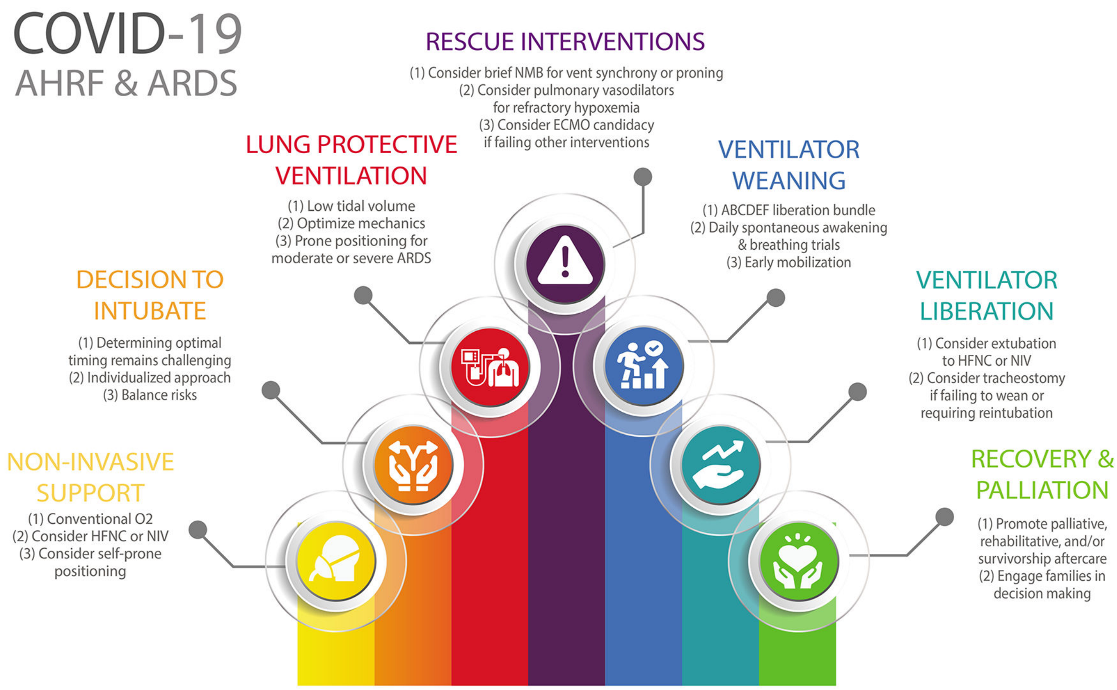

Figure 1.

Management of AHRF and ARDS in COVID-19 patients largely mirrors that for non-COVID-19 etiologies. Patients with COVID-19 may require airborne infectious precautions and other special considerations to minimize risk of viral transmission to healthcare workers. Though made challenging by limited visitation policies, family engagement remains essential throughout the course of critical illness. Adherence to critical care best practices under adverse conditions is key. Abbreviations: AHRF, acute hypoxemic respiratory failure; ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation (including continuous positive airway pressure and bilevel positive airway pressure ventilation); NMB, neuromuscular blockade. Figure adapted from sticker2you/stock.adobe.com. Icon illustrations from thenounproject.com: “Oxygen mask,” by Sergey Demushkin; “Split,” by ImageCatalog; “Ventilator,” by Luis Prado; “Improve,” “Trending,” and “Care,” by Adrien Coquet.