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A Nurse's Guide to COVID-19

An evidence-based review of the care of hospitalized adults with this disease.

ABSTRACT: To assist nurses caring for hospitalized adults with coronavirus disease 2019 (COVID-19), the authors synthesize evidence-based information on the disease, providing background on the epidemiology and history of severe acute respiratory syndrome coronavirus 2, the causative virus. They also discuss the risks for severe effects of the illness, the multiple signs and symptoms hospitalized adults with COVID-19 may manifest, and the precautions hospitals should take to keep health care providers and patients safe during the course of this pandemic.

Keywords: coronavirus disease 2019, COVID-19, infection control, pandemic, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

On December 31, 2019, Chinese authorities alerted the World Health Organization (WHO) that a pneumonia of unknown etiology had been identified in several people in the city of Wuhan, China.[1] Although the causal agent wasn't known at that time, it would later be identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19). Over the next several months, as the virus spread throughout the world, scientists, medical professionals, and researchers struggled to control this highly contagious disease, while exploring potential treatments and working to develop a safe and effective vaccine. By March 11, 2020, the WHO declared that COVID-19 had reached pandemic proportions.[2]

Within eight months, potential remedies began to emerge. On November 10, 2020, the U.S. Food and Drug Administration (FDA) issued an emergency use authorization (EUA) permitting the Eli Lilly monoclonal antibody bamlanivimab to be administered to adults and pediatric patients ages 12 and older who tested positive for SARS-CoV-2 and were at high risk for progressing to severe disease or hospitalization.[3] Shortly thereafter, three potential vaccines developed by Pfizer and BioNTech,[4] Moderna and the National Institute of Allergy and Infectious Diseases,[5] and the University of Oxford working with AstraZeneca[6] made headlines for having achieved promising interim safety and efficacy results in clinical trials, though the Pfizer and Moderna vaccines were said to face potential storage and distribution challenges due to the extremely cold temperatures required for safe storage.[7] That same month, the FDA granted an EUA for a second COVID-19 treatment to be used in patients ages 12 and older who have mild to moderate disease and are at high risk for developing more severe symptoms: a therapy developed by Regeneron that combines the monoclonal antibodies casirivimab and imdevimab.[8] On December 11, 2020, the FDA issued an EUA for the Pfizer–BioNTech vaccine, shipments of which left a Michigan facility on December 13 in order for U.S. distribution and administration to begin that same week.[9,10] Scientists' understanding of the disease, optimal treatment, and effective preventive strategies has evolved rapidly.

Until vaccines are widely available and administered in sufficient numbers to contain the pandemic, health care facilities will be challenged to obtain adequate resources, including personal protective equipment (PPE), cleaning supplies, hospital beds, ventilators, and medications, while maintaining suf-

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ficient health care staff. Nurses will play a vital role in managing the disease in hospitalized adults and in promoting health and safety throughout their communities. This article synthesizes the evidence-based information available when we went to press in January to assist nurses caring for hospitalized adults with COVID-19.

EPIDEMIOLOGY

SARS-CoV-2 is in the family of coronaviruses that includes SARS-CoV, initially associated with civets and raccoon dogs, and Middle East respiratory syndrome coronavirus, associated with dromedaries and bats.[11] Coronaviruses are ribonucleic acid (RNA) zoonotic viruses that normally exist in animals but can infect and spread among humans. The WHO has not yet identified the animal source of SARS-CoV-2, though it is suspected that the virus resides mainly in bats.[12]

Respiratory, or droplet, transmission of SARS-CoV-2 occurs when an infected person (whether symptomatic or asymptomatic) coughs, sneezes, talks, sings, or breathes within approximately six feet of a noninfected person, dispersing viral secretions that are inhaled into the nose, mouth, airways, or lungs.[13]

Airborne transmission can occur when infectious droplet nuclei are aerosolized, or dispersed and suspended in air over long distances and for long periods: during aerosol-generating medical procedures, such as suctioning or intubation, for example, and even in the absence of such procedures in poorly ventilated indoor settings.[12]

Fomite transmission. Infection through contact with contaminated surfaces is considered a potential mode of SARS-CoV-2 transmission because the virus has been found to survive on certain surfaces for periods ranging from hours to days, it has been consistently found on surfaces in the vicinity of infected patients, and other coronaviruses are transmitted via contact with fomites.[12] There are, however, no confirmed reports of fomite transmission of SARS-CoV-2,[12] and contact with contaminated surfaces is not considered a major source of transmission, though people may become infected with the virus if they touch a contaminated surface and then touch their nose, mouth, or eyes.[13]

The incubation period for SARS-CoV-2 is generally believed to be 14 days,[14] though viral RNA can be detected one to three days before symptoms develop and asymptomatic carriers can transmit the virus.[12] While the viral load tends to be highest upon symptom onset and gradually declines over one to three weeks, in patients with severe disease it can persist much longer.[12]

Risk factors for COVID-19. People of all ages are at risk for COVID-19 infection and severe disease, but people age 65 or older and those living in a nursing home or long-term care facility are more likely to die from the disease. The Centers for Disease Control and Prevention (CDC) reports that in states with available data on assisted-living facilities, an average of one in five residents with COVID-19 had died as of October 15, 2020, compared with one in 40 people with COVID-19 in the general population.[15]

Behavioral risks and underlying conditions. Regardless of age, smokers and people with the following underlying conditions are at risk for more severe illness from COVID-19, especially when the conditions are not well controlled[16]:

- hypertension
- cardiovascular disease
- diabetes
- chronic obstructive pulmonary disease
- cancer
- chronic renal disease
- obesity
- sickle cell disease

Pregnant women are also at risk for more serious illness from COVID-19.[16]

CLINICAL PRESENTATION

While many people with COVID-19 experience few or no symptoms, others develop respiratory and circulatory collapse.

A U.S. case surveillance report on 1,320,488 confirmed COVID-19 cases found that of the 373,883 patients for whom symptom data were available, 70% had experienced fever, cough, or shortness of breath; 36% had muscle aches; 34% reported headaches; and 8% lost sense of taste or smell.[17] Other reported symptoms included diarrhea, rhinorrhea, sore throat, abdominal pain, nausea, and vomiting.

Cardiac manifestations have been noted in many patients with COVID-19, whether direct or due to demand ischemia or cytokine-mediated cardiomyopathy. These patients present with the same signs and symptoms as other COVID-19 patients and rarely report chest pain, but they tend to have elevated levels of such biomarkers as creatine kinase–myocardial band, troponin I, and N-terminal pro-B-type natriuretic peptide, as well as an elevated leukocyte count.[18]

Dermatologic and ophthalmic symptoms. Patients with less severe COVID-19 may develop painful, itchy lesions on their feet and, less commonly, their hands that resemble chilblains and are sometimes referred to as "COVID toes."[19] It is unclear whether this condition is a direct result of COVID-19 or is related to sedentary behavior or failure to wear warm footwear when curfews or restrictions on social gatherings and out-of-home activities are in place.

Some patients with COVID-19 develop ophthalmic symptoms, often called "COVID eyes," which include conjunctivitis, excessive tearing or discharge, and light sensitivity, ranging from mild to severe. Such symptoms are more common in patients with severe disease.[19]

CATEGORIES OF ILLNESS

The National Institutes of Health (NIH) has developed the following categories of illness severity that guide the management of COVID-19 based on a patient's clinical status[20]:

- *Asymptomatic or presymptomatic infection*–patients test positive for SARS-CoV-2 by virologic diagnostic testing using a real-time reverse transcription polymerase chain reaction test or an antigen test but have no symptoms.
- *Mild illness*–patients have any number of the various signs and symptoms of COVID-19, such as fever, cough, sore throat, malaise, headache, or muscle pain, but have normal chest imaging and experience no shortness of breath or dyspnea. For many, COVID-19 can be managed at home. The NIH makes no specific recommendations for immunomodulatory or antiviral therapy in these patients, though it recommends against the use of dexamethasone.

Patients entering hospitals through EDs should be screened for COVID-19 symptoms, and if present, they should be tested for SARS-CoV-2 antigens prior to transfer to a general unit.

- *Moderate illness*–patients have evidence of lower respiratory disease by clinical assessment or imaging but maintain an oxygen saturation by pulse oximetry (SpO_2) level of at least 94% on room air at sea level.
- *Severe illness*–patients have a respiratory rate of more than 30 breaths per minute, an SpO_2 level of less than 94% on room air at sea level, a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO_2:FiO_2) of less than 300 mmHg, or a more than 50% lung involvement on imaging.
- *Critical illness*–patients have respiratory failure and septic shock, with or without multiple organ dysfunction.

PHARMACOLOGICAL MANAGEMENT IN HOSPITALIZED ADULTS

For hospitalized patients with COVID-19 who require supplemental oxygen, the NIH pharmacological recommendations vary with the method of oxygen delivery.[20]

For patients requiring conventional oxygen therapy (not delivery through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]), administer one of the following:

- *If oxygen requirements are minimal*, remdesivir 200 mg IV on day 1 followed by remdesivir 100 mg IV once daily for up to four days or until hospital discharge. In an inpatient acute care setting, treatment can continue for up to 10 days if there is no improvement by day 5.
- *If oxygen requirements are increasing*, dexamethasone 6 mg IV or by mouth for up to 10 days or until hospital discharge, plus remdesivir at the dosage described above.
- *If remdesivir is unavailable or cannot be used*, the dexamethasone regimen may be used alone.

For patients requiring oxygen delivery through a high-flow device or noninvasive ventilation, administer dexamethasone alone at the dosage described above or dexamethasone plus remdesivir at the dosages described above.

For patients requiring invasive mechanical ventilation or ECMO, administer dexamethasone alone at the dosage described above or, for recently intubated patients, the dexamethasone-plus-remdesivir regimen described above. Remdesivir alone is not recommended for recently intubated patients.

For patients with moderate disease not requiring supplemental oxygen, the NIH makes no specific recommendations for the use of remdesivir but notes it may be appropriate in patients at high risk for disease progression. The NIH recommends against the use of dexamethasone in these patients.

For more on how remdesivir and dexamethasone came to be used to treat patients with COVID-19, see *Remdesivir Use in COVID-19*[20-23] and *Corticosteroid Therapy for COVID-19*.[20, 24, 25]

Remdesivir Use in COVID-19

The investigational antiviral agent remdesivir was initially developed for the treatment of the Ebola and Marburg viruses. Its safety and efficacy in hospitalized adults with COVID-19 was evaluated in the large randomized, double-blind, placebo-controlled Adaptive COVID-19 Treatment Trial.[20] The trial was stopped early by the National Institute of Allergy and Infectious Diseases, which determined that the need to collect more definitive evidence was outweighed by the ethical responsibility to provide a potentially lifesaving treatment, rather than a placebo, to patients with COVID-19, since early results had shown a benefit with remdesivir.[21]

On May 1, 2020, the Food and Drug Administration (FDA) issued an emergency use authorization allowing remdesivir to be distributed in the United States and administered by health care providers to adults and children hospitalized with suspected or confirmed COVID-19.[22] On October 22, 2020, remdesivir became the first antiviral drug approved by the FDA "for adults and pediatric patients (12 years and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization."[23]

PREVENTING THE SPREAD OF COVID-19 IN HOSPITALS

Screening at admission. Patients entering hospitals through EDs should be screened for symptoms of COVID-19, and if symptoms are present, they should be tested for SARS-CoV-2 antigens prior to transfer to a general unit. If patients have respiratory symptoms, chest radiographs and computed tomographic (CT) scans of the chest may be ordered, as certain lung patterns on chest X-ray and CT scan may indicate the presence of COVID-19. These include lobe consolidation, most commonly in the right lower lobe though it can occur in any or all lobes. CT scans may reveal abnormalities even in asymptomatic patients.[26] COVID-19 pneumonia tends to progress rapidly (within one to three weeks) from focal unilateral ground-glass opacities to diffuse bilateral ground-glass opacities with coexisting consolidations.[26, 27] Pan and colleagues studied CT findings in patients with COVID-19 at four-day intervals from symptom onset through recovery and found that the number and severity of pulmonary lesions increased over the first 10 days, then plateaued and gradually decreased.[27]

Isolation. Patients with COVID-19 should be placed in isolation, using contact and droplet precautions. American Nurses Association guidance on crisis standards of care states that hospitals and other health care institutions "have a duty to safeguard employees with policies and practices that are evidence-based, transparently decided and have clear accountabilities."[28] To that end, health care

Corticosteroid Therapy for COVID-19

The United Kingdom–based Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial, in which patients were randomized to receive dexamethasone or usual care (or another treatment, including, among others, hydroxychloroquine and convalescent plasma), found that the mortality rate was significantly lower among patients assigned to receive dexamethasone than among those receiving usual care.[24] Based on the preliminary, unpublished results of this trial, the National Institutes of Health (NIH) recommends dexamethasone treatment for hospitalized patients with COVID-19 who require supplemental oxygen. If dexamethasone is not available, the NIH recommends using alternative glucocorticoids, such as prednisone, methylprednisolone, or hydrocortisone.[20] The NIH may modify these recommendations based on the final published results of ongoing studies.

While receiving systemic corticosteroids, patients should be assessed for hypertension and fluid retention; hyperglycemia; arrhythmias, such as atrial fibrillation or flutter; gastritis; ulcers; gastrointestinal bleeding; bone and muscle deterioration; and neuropsychiatric effects, including psychosis, delirium, confusion, or disorientation.[25]

systems must develop preparedness plans that ensure all staff receive the highest level of protection when providing patient care and are aware of current evidence-based infection control procedures for the early identification, containment, and care of patients with symptoms of COVID-19. The CDC has published information for health care providers on screening options, PPE and training, environmental infection control, hand hygiene, aerosol-generating procedures, and patient placement (see www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html).

Discontinuing isolation. Current criteria for discontinuing isolation without requiring retesting are as follows[29]:

- for symptomatic patients, 10 days after symptom onset plus at least three additional days without symptoms, including fever and respiratory symptoms
- for asymptomatic patients, 10 days after testing positive for SARS-CoV-2

Aerosol-generating procedures. While droplet and contact precautions should be practiced by all providers caring for patients with COVID-19 and by the patients themselves, the WHO recommends that health care providers wear N95, FFP2, or FFP3 respirators, if available (or medical masks when respirators are in short supply),[30] when participating in any aerosol-generating procedure, including endotracheal intubation, bronchoscopy, open suctioning, administration of a nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from a ventilator, noninvasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation.[30] In addition to the WHO recommendations, the CDC suggests prioritizing airborne infection isolation rooms for patients undergoing such procedures and advises providers to use eye protection (goggles or a face shield) during both aerosol-generating procedures and surgeries involving the nose, throat, oropharynx, or respiratory tract.[31]

Transport of patients with presumed or confirmed SARS-CoV-2 infection should occur only if absolutely necessary. Medical procedures should be performed in the patient's room when possible. If patient transport is necessary, the patient should wear a face mask to contain respiratory droplets.[31]

Shortages of PPE. Because of the scarcity of PPE, most notably N95 respirators, some facilities have instituted FDA-authorized practices for N95 decontamination by vaporized hydrogen peroxide gas plasma, which allows for reuse.[32] The Infectious Diseases Society of America has published eight recommendations on the use of PPE for preventing infection of health care personnel caring for patients with suspected or confirmed COVID-19.[33] Using the Institute of Medicine's crisis standards of care framework,[34] the recommendations address the use of gloves, shoe covers, surgical masks, face shields, N95 respirators, and reprocessed N95 respirators.[33] The current pandemic and the subsequent documented shortages of PPE across health care settings, rather than evidence-based practice, drives many of these recommendations.[33]

OXYGEN THERAPY

Hypoxemia is common in hospitalized adults with COVID-19. Care of these patients usually begins with standard oxygen therapy and continuous SpO2 monitoring. If a patient's SpO2 level is greater than 92% and the patient has no symptoms of respiratory distress, supplemental oxygen is unnecessary and should be discontinued, as it can increase aerosolization of droplet particles, escalating provider risk of infection. Adults with COVID-19, however, often develop acute hypoxemic respiratory failure, rendering conventional oxygen therapy insufficient.

Oxygen saturation should be maintained between 92% and 96%. High-flow oxygen via nasal cannula is recommended, but if it's unavailable and the patient doesn't require intubation, a trial of noninvasive positive-pressure ventilation is suggested. Currently, the use of a noninvasive positive-pressure ventilation helmet device is not recommended for patients with COVID-19 as there are insufficient data to prove its safety or efficacy.[35]

Intubation. For adults who develop acute hypoxemic respiratory failure, conventional oxygen

therapy may be insufficient. In such cases, use of high-flow oxygen via nasal cannula or noninvasive positive-pressure ventilation is recommended over intubation, but if patients experience rapid deterioration with increased oxygen requirements, intubation may be indicated to reduce risk of progression to acute respiratory distress syndrome (ARDS), especially if the patient has additional acute organ dysfunction or chronic comorbidities, or if high-flow oxygen via nasal cannula or noninvasive positive-pressure ventilation are unavailable.[20]

Mechanical ventilation. When patients with COVID-19 develop ARDS and require mechanical ventilation, the NIH and the Surviving Sepsis Campaign (SSC) recommend using low tidal volumes (4 to 8 mL/kg of predicted body weight) over higher tidal volumes (more than 8 mL/kg), targeting plateau pressures of less than 30 cm H_2O.[20, 35]

A large number of patients with COVID-19 and ARDS require sedation during mechanical ventilation to reduce ventilator dyssynchrony, thereby improving oxygenation and decreasing the risk of lung trauma.[36] Sedation requirements are unusually high in many patients with COVID-19. A high respiratory drive and intense inflammatory responses have been linked to tolerance of certain medications, requiring the use of multiple agents. Other factors that may boost sedation requirements include younger age and prior good health. Nurses should monitor sedated patients for potential adverse effects, including hypotension, QT prolongation, hypertriglyceridemia, and delirium.[36]

For adults with COVID-19 and moderate to severe ARDS, the NIH and SSC recommend the use of a positive end-expiratory pressure greater than 10 cm H_2O, with clinicians monitoring patients for barotrauma and hypotension.[20, 35] Both peak and plateau pressures should be monitored for acute elevations.

For adults with COVID-19, severe ARDS, and hypoxemia despite optimized ventilation and other rescue strategies, the NIH and SSC recommend using an inhaled pulmonary vasodilator as rescue therapy, which should be tapered off if oxygenation fails to improve rapidly.[20, 35]

If ventilator dyssynchrony persists despite maximum sedation, the NIH recommends initiating intermittent boluses of neuromuscular blocking agents to support protective pulmonary ventilation.[20, 35] If intermittent boluses of these agents are ineffective, a continuous infusion can be used for up to 48 hours as long as patient anxiety and pain can be adequately monitored and controlled.[20, 35]

The Society of Critical Care Medicine recommends avoiding the use of bag-valve-mask ventilation in patients with COVID-19, if possible.[37] When bag-valve-mask ventilation is necessary, the patient should be intubated using rapid sequence intubation by an experienced provider and high-efficiency particulate air filtration to limit viral spread.

PRONE POSITIONING

To improve oxygenation in patients with COVID-19 and persistent hypoxemia despite increasing supplemental oxygen delivery, the NIH recommends considering a trial of awake prone positioning, provided endotracheal intubation is not otherwise indicated.[20] However, awake prone positioning should not be used as a rescue therapy for refractory hypoxemia in order to avoid intubating patients for whom mechanical ventilation is clearly indicated.[20]

For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, the NIH recommends 12 to 16 hours per day of prone ventilation.[20]

To reduce the risk of peripheral nerve injury associated with prone positioning in COVID-19–related ARDS, try to reduce physical stress on the peripheral nerves, avoiding prolonged focal compression and stretching, and consider providing protection for the elbow, upper arm, and shoulder.[38]

Invasive lines should be placed on the same side as any tubes, if possible, and monitored closely to prevent dislodgment. Skin, particularly at the head and knees, is at high risk for breakdown and should be assessed frequently.

ECMO GUIDELINES

ECMO, in which venous blood is pumped through an artificial oxygenating membrane before returning to the venous circulation, may provide short-term rescue therapy to patients with refractory hypoxemia and severe ARDS. The Extracorporeal Life Support Organization (ELSO) has stated that the decision to initiate ECMO in a patient with COVID-19 and severe refractory ARDS should be made on a case by case basis and "reassessed regularly based on overall patient load, staffing, and other resource constraints, as well as local governmental, regulatory, or hospital policies."[39]

ECMO is resource intensive and requires highly specialized management. Data on ECMO and COVID-19–related ARDS are limited, though research regarding clinical outcomes with the use of ECMO in this context is ongoing. ELSO acknowledges that ECMO teams may need to be very selective in determining a patient's suitability for ECMO given limited resources, but practice should be consistent with the existing indications and contraindications for ECMO in COVID-19–infected adults.[40]

In addition to following interim ECMO guidelines, ELSO recommends maximizing traditional ARDS therapies, specifically prone positioning, prior to initiating ECMO.[40] Clinicians working in facilities that have no access to ECMO or mobile ECMO can consider referring patients to an ECMO center.

CRITICAL ILLNESS MANAGEMENT

Septic shock. When a patient with COVID-19 develops septic shock, the NIH suggests following the SSC guidelines, which recommend using buffered, balanced crystalloids for fluid resuscitation and assessing such dynamic parameters as capillary refill, skin temperature, and serum lactate levels to determine fluid responsiveness.[20, 35]

When initiating vasopressors in adults with COVID-19 who are in septic shock, norepinephrine is the drug of choice, followed by vasopressin, which can be added rather than further escalating the norepinephrine dose.[35] If inotropic support is necessary in patients with impaired cardiac function, dobutamine is recommended.[20]

For adults whose shock is refractory to vasopressor therapy, initiate systemic corticosteroids if they are not already being administered to treat COVID-19.[20]

Acute kidney injury. An estimated 22% of patients admitted to ICUs with COVID-19 develop acute kidney injury requiring renal replacement therapy (RRT).[20] The NIH suggests that the same indications for RRT used in other critically ill patients should be used in patients with COVID-19.[20] The American Society of Nephrology has released recommendations that would enable hospitals to administer RRT to patients with acute kidney injury in a safe and timely manner while limiting exposure to staff.[41]

When biocontainment is necessary, continuous RRT (CRRT), if available, is preferable to intermittent hemodialysis, which requires 1:1 nursing support.[41] If hemodialysis nurses set up and troubleshoot the equipment, setup can occur outside the patient's room or the ICU isolation room and an ICU nurse can take the machine into the room and connect it to the patient, minimizing exposure and use of PPE.

If CRRT capacity is overwhelmed by COVID-19 surge, CRRT machines can be run with higher flow rates over shorter periods and then disinfected for use with other patients.[41] Patients with suspected or confirmed COVID-19 admitted to non–critical care units should not be transported to a general dialysis unit for treatment.[41] In institutions that sequester COVID-19 patients on a dedicated floor, video monitoring can enable one dialysis nurse to monitor up to three patients during intermittent hemodialysis.[41]

Coagulopathies. In advanced COVID-19, the systemic inflammatory response may trigger thrombotic events such as pulmonary embolisms, venous thromboembolisms (VTEs), and thromboembolic strokes. When Klok and colleagues investigated the incidence of thrombotic complications in patients with COVID-19 admitted to the ICU of three Dutch hospitals, they found a cumulative incidence of 31%, including a 27% incidence of VTE (confirmed by diagnostic imaging), despite standard thromboprophylaxis.[42]

When nurses identify and notify the attending practitioner of signs and symptoms that could indicate thrombotic complications in patients with COVID-19, such as pain, pallor, or paresthesia in a limb; chest pain; severe abdominal pain; sudden confusion; loss of balance; or hemiplegia, it may speed the ordering of appropriate testing and treatment.

Convalescent plasma for COVID-19 is not approved by the FDA, though the agency provides guidance for its use in treating hospitalized patients with COVID-19 under an EUA.

Hematologic and coagulation parameters, such as D-dimer, prothrombin time, platelet count, and fibrinogen, are commonly measured in hospitalized patients with COVID-19, though there are currently insufficient data to guide management decisions. Tang and colleagues analyzed the 28-day mortality of patients with severe COVID-19 and its correlation with heparin use and patients' coagulopathy risk as determined by D-dimer and sepsis-induced coagulopathy (SIC) score, which is based on prothrombin time, platelet count, and the sequential organ failure assessment (SOFA) score.[43] While the 28-day mortality rate among heparin users overall was not significantly different than that among nonusers, for patients with higher coagulopathy risk based on an SIC score of 4 or higher, or D-dimer more than six times the upper limit of

normal, the 28-day mortality rate was lower among those who used heparin than among those who did not. Based on this study and others, the International Society on Thrombosis and Haemostasis (ISTH) suggests it may be useful to monitor prothrombin time, fibrinogen, platelet count, and D-dimer to aid in patient prognosis.[44]

Both the NIH and the ISTH recommend that hospitalized adults with COVID-19 receive VTE prophylaxis with either unfractionated heparin or low-molecular-weight heparin per the standard of care for other hospitalized adults.[20,44] Patients receiving anticoagulant or antiplatelet therapy prior to COVID-19 diagnosis should continue that therapy; there are currently insufficient data to recommend for or against the use of therapeutic doses of antithrombotic or thrombolytic agents in COVID-19, however clinical trials are currently underway.[20]

If a patient with COVID-19 is suspected of having a thromboembolic incident, and confirmative imaging is not an option, the patient should receive therapeutic doses of anticoagulant therapy in accordance with guidelines set for hospitalized patients without COVID-19.[20] Institutional policies should also guide antithrombotic therapy in patients with COVID-19 who require ECMO or CRRT or whose catheters or extracorporeal filters have thrombosed.[20]

INVESTIGATIONAL AGENTS AND OFF-LABEL USE

In addition to the use of agents granted EUAs, such as Eli Lilly and Regeneron's monoclonal antibody COVID-19 treatments, clinicians can access and prescribe investigational drugs approved for other indications through compassionate use or expanded access programs by completing an emergency investigational new drug (IND) application or through off-label use. Several drugs approved for other indications and multiple investigational agents have been or are currently being studied as potential treatments for COVID-19 in clinical trials worldwide.

The antimalarial drugs chloroquine and hydroxychloroquine were initially granted EUAs by the FDA for the treatment of COVID-19, but these were revoked in June 2020 as clinical studies cast doubt on their efficacy.[45] The NIH also recommended against the use of these drugs, either with or without azithromycin, to treat COVID-19 in hospitalized patients or in nonhospitalized patients outside of a clinical trial.[20]

Protease inhibitors. The NIH recommends against using lopinavir–ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in clinical trials.[20] The NIH recommendation is based on the lack of evidence that lopinavir–ritonavir or other HIV protease inhibitors could achieve concentrations that would inhibit the SARS-CoV-2 proteases and the fact that lopinavir–ritonavir demonstrated no efficacy against COVID-19 in a moderately sized randomized controlled trial.[20]

Convalescent plasma is separated from the blood of a person who has developed antibodies to the pathogen of concern. Convalescent plasma for COVID-19, obtained from people who have recovered from the disease, contains antibodies to SARS-CoV-2.

Convalescent plasma for COVID-19 is not approved by the FDA, though the agency provides guidance for its use in the treatment of hospitalized patients with COVID-19 under an EUA (see www.fda.gov/media/141479/download) or as an emergency IND (see www.fda.gov/media/136798/download, which also includes guidance on requesting emergency IND applications). An IND application allows convalescent plasma to be used in patients with confirmed COVID-19, and serious or life-threatening disease.[46]

Immunomodulators. Both interleukin-1 (IL-1) and interleukin-6 (IL-6) inhibitors are currently undergoing trials in the treatment of COVID-19. Researchers propose that these drugs inhibit the cytokine release that occurs in COVID-19, thereby reducing associated lung damage. According to the NIH, there are insufficient data to support or oppose the use of IL-1 inhibitors, such as anakinra, and recommends against the use of the anti-IL-6 receptor monoclonal antibodies sirilumab and tocilizumab or the anti-IL-6 monoclonal antibody siltuximab in the treatment of COVID-19, outside of clinical trials.[20]

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). As researchers discover more about SARS-CoV-2, concern has arisen surrounding ACE inhibitors. ACE inhibitors cause increased expression of the ACE2 receptor, which is a binding site for SARS CoV-2, leading to a theoretical risk of increased viral access to target cells.[47] There is, however, no evidence of either harm or benefit to patients taking ACE inhibitors as related to COVID-19.[47]

The American Heart Association, American College of Cardiology, and Heart Failure Society of America all recommend continuing ACE inhibitors in patients currently prescribed these drugs for indications such as heart failure, hypertension, or ischemic heart disease. If such patients are diagnosed with COVID-19, treatment decisions should take into account the hemodynamic status and clinical presentation of the individual patient,[48] because the risk of adverse events may be higher with discontinuation. The NIH recommends that patients with COVID-19 who are prescribed ACE inhibitors or ARBs for cardiovascular disease (or other indications) should continue taking these medications.[20]

The NIH, however, recommends against the use of ACE inhibitors or ARBs for treating COVID-19 outside the setting of a clinical trial.

HOSPITAL DISCHARGE

As hospital capacity is increasingly overwhelmed by patients treated for COVID-19, patients can be discharged home when clinically indicated, with the decision made by the patient's clinical care team in consultation with state or local public health officials.[49] The decision should take into account the type of home (for example, private home versus long-term care facility), whether transmission precautions are still required, and the ability of the patient to follow recommendations for infection control and prevention. If transmission precautions are still required, the patient would ideally be discharged to a facility that can safely accommodate patients infected with SARS-CoV-2 in which the patient would be sequestered in an area with others infected with the virus.[49] If transmission precautions have been discontinued, no further discharge restrictions would apply.[49]

Discontinuing transmission precautions. Current evidence suggests that patients often continue to shed detectable SARS-CoV-2 RNA when they are no longer infectious.[49] For this reason, the CDC supports the use of a symptom-based, rather than a testing-based, strategy for determining whether transmission precautions can be discontinued for patients who have been treated for COVID-19.[50] A symptom-based approach not only limits unnecessary isolation but also preserves laboratory testing resources.

The symptom-based strategy is built on the NIH categories of illness described earlier[47] and is informed by unpublished data from studies that measured the degree to which concentrations of SARS-CoV-2 RNA in upper respiratory specimens declined over time after symptom onset.[50] The CDC suggests that clinicians consider the highest level of illness severity patients experience throughout their clinical course in order to determine the duration of transmission precautions.[49]

For patients with mild to moderate illness who are not severely immunocompromised, the CDC suggests discontinuation of transmission precautions after at least 10 days have passed since first symptoms appeared and at least 24 hours have passed since last fever without use of an antipyretic medication, and after respiratory symptoms have improved.[49]

For patients with severe to critical illness and those who are severely immunocompromised, the CDC suggests waiting at least 10 to 20 days after first symptoms appeared and at least 24 hours after last fever without use of an antipyretic medication, given that respiratory symptoms have improved.[49] Consultation with infection control experts may be in order.[49]

A test-based strategy may be considered for severely immunocompromised patients if, in consultation with local infectious disease experts, concerns are raised that the patient may remain infectious for more than 20 days or for patients in whom there is reason to believe a test-based strategy will allow for earlier discontinuation of transmission precautions than the symptom-based strategy.[49]

The long-term effects of COVID-19 are not fully understood at this point, though it's believed the disease may cause permanent lung and heart damage.

LONG-TERM SEQUELAE

The long-term effects of COVID-19 are not fully understood at this point, though it's believed the disease may cause permanent lung and heart damage. Pulmonary fibrosis, which can prolong mechanical ventilation and hospitalization, is a known irreversible complication of ARDS, regardless of etiology.

Long-term heart damage secondary to COVID-19 infection is also a concern. A German study evaluated cardiac magnetic resonance imaging of 100 survivors of COVID-19 and found that 78 had evidence of cardiac involvement, while 60 had ongoing inflammation independent of preexisting conditions.[51]

END-OF-LIFE CARE

End-of-life discussions are always an important part of patient care and should occur early in the hospital admission process, particularly during a pandemic in which the U.S. death toll has surpassed 400,000. Advanced directives should be established by the patient

on admission, and palliative care providers should be consulted early, as they can help guide, educate, comfort, and aid in the complex decision-making required during this time. Not only can these providers offer comfort at the end of life, but they can also help support families isolated from their loved ones due to COVID-19 infection prevention and control measures, including the limited or no-visitation hospital policies that mean patients frequently die alone. Nurses can help improve the social connection between loved ones by aiding in and encouraging video calls with family and friends. Telephone and video calls using tablets are important for communication and for psychosocial and spiritual support, which may provide some closure for family members and peace of mind for the patient. ▼

For 13 additional nursing continuing professional development activities on the topic of COVID-19, go to www.nursingcenter.com.

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