COVID-19
Critical care management of adult patients with COVID-19 infection
Version History

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Further Information

For more information on COVID see the COVID guidance section of our website, www.gov.scot/coronavirus.
Covid-19: Guidance on critical care management of adult patients

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1. Introduction

The purpose of this guideline is to provide NHS Scotland with advice regarding the clinical management of critically ill patients with COVID-19 infection.

This guideline has been produced for:
- Healthcare practitioners working in critical care environments
- Staff involved in the planning and delivery of critical care services for the Scottish population

This guideline focuses on the clinical management of critically-ill patients with COVID-19 infection. For guidelines detailing the clinical management of all patients with suspected or confirmed COVID-19 infection, please see the Scottish Government’s Clinical Advice.

These recommendations have been developed in response to a rapidly changing global pandemic and are based on the currently available evidence and expert opinion, with rapid peer review as assurance. This guidance will be reviewed further as evidence-based care for COVID-19 positive patients becomes more established.

For case definitions please refer to the Health Protection Scotland (HPS) Guidance for Secondary Care.
2. Clinical Context

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is the pathogenic organism leading to COVID-19 disease\(^1\). Transmission predominantly occurs through respiratory droplet spread between individuals or direct contact with fomites on contaminated surfaces\(^1\).

The clinical spectrum of COVID-19 disease is wide, from asymptomatic infection to severe pneumonia and the development of multiple organ failure leading to death. Approximately 5\% of patients with confirmed SARS-CoV-2 infection requiring hospital admission become critically ill\(^2\). Several risk factors for progression to critical illness have been identified, including increasing age\(^3\), obesity\(^4\), male gender\(^5\), Black and Asian ethnicity\(^6\), low socio-economic status\(^7\) and the presence of chronic co-morbidity\(^4\).

COVID-19 disease may lead to the development of severe hypoxaemic respiratory failure, with most patients fulfilling the Berlin Criteria\(^8\) for diagnosis of Acute Respiratory Distress Syndrome (ARDS). As a new disease, the pathophysiology of COVID-19 is not yet fully understood. Although controversial, two distinct clinical phenotypes of respiratory failure in COVID have been proposed, which may occur in sequence\(^9\). Early in the disease course, it is proposed that some patients have an atypical viral pneumonitis with severe hypoxaemia with relative preservation of compliance and a low ventilation - perfusion (V: Q) ratio. This subsequently progresses into a more classic "ARDS" phenotype, as defined by the Berlin Criteria\(^8\), with poor compliance, high lung weight, and the potential for recruitment.

In addition to respiratory failure, multi-system involvement is common in COVID-19 disease, with over 25\% of patients developing cardiovascular failure, and over 30 \% suffering an acute kidney injury necessitating renal replacement therapy\(^10\). Patients with COVID-19 disease are also recognised to be at increased risk of arterial, venous and pulmonary thromboembolism, the mechanisms of which are not fully understood\(^11\). SARS-CoV-2 infection has also been associated with the development of a potentially severe inflammatory syndrome in children called paediatric multisystem inflammatory disorder (PIMS)\(^12\).

Initial outcome data for the critically ill Scottish Population with confirmed COVID-19 disease indicates a 30-day mortality of 39\%, which is increased in those receiving advanced respiratory support, older patients, and those requiring multiple organ support\(^13\). The long-term sequelae of COVID-19 survivors are currently unknown. Guidance for the longer term recovery needs of COVID-19 survivors is currently being developed and when published will be signposted within this document.
3. Escalation to Critical Care and Ethical Decision Making

Assessment for escalation of care to a critical care environment with invasive organ support should take a holistic approach incorporating individual assessment of frailty, comorbidity, severity of illness, and the likelihood of critical care provision leading to survival where quality of life is deemed acceptable to the patient. Where possible, decisions regarding escalation of care and quality of life should be carried out collaboratively with patients, their families and the referring clinical team, taking into account individual patient circumstances and with respect to ethical principles.

Further guidance regarding assessment for critical care admission can be found in the Scottish Government’s COVID-19 Clinical Advice.

For guidance on ensuring an ethical approach to decision making, please see the Scottish Government’s Ethical Advice and Support Framework.
4. Clinical Management of Patients with COVID-19 Infection

4.1 Aerosol Generating Procedures (AGP) in Patients with COVID-19 Infection

Aerosols are produced when an air current moves across the surface of a film of liquid. Airway and ventilation interventions in patients with SARS-CoV-2 infection may result in the generation of aerosolised particles. AGPs can produce airborne particles <5 μm in size which can remain suspended in the air, travel over a distance and may cause infection if they are inhaled.

AGPs are any medical and patient care procedure that results in the production of airborne particles. AGPs create an increased risk of transmission of infection, both to healthcare workers, and other patients\textsuperscript{14}. A current list of interventions classified as AGPs can be found \textit{here}.

In mechanically ventilated patients circuit connections should be regularly checked. Clinical vigilance should be employed to avoid unplanned circuit disconnections during high risk interventions such as turning and transfers.

4.2 The Management of COVID-19 Related Respiratory Failure

4.2.1 Supplemental Oxygen Therapy

The aim of supplemental oxygen therapy in patients with COVID-19 disease is to support adequate oxygenation for physiological processes while avoiding hyperoxaemia, which may be harmful\textsuperscript{15}.

For patients without pre-existing lung disease, an SpO\textsubscript{2} target of 92-96% is appropriate, when used in collaboration with clinical vigilance for deterioration.

Saturation targets can be individualised for patients and may be lower in patients with underlying lung disease such as chronic obstructive pulmonary disease.

In an awake and co-operative patient on oxygen or non-invasive ventilatory support (see below), a trial of awake proning should be considered, as tolerated by the patient. The physiological basis for this is through recruitment of the dependent areas of the lung and improved secretion clearance, and there is a strong evidence base for proning in ventilated patients with moderate to severe ARDS\textsuperscript{16}. The utility for this in non-ventilated patients is as yet unproven, but there have been anecdotal reports of improved oxygenation with this technique\textsuperscript{17}.
4.2.2 Non-Invasive Ventilatory Support in Patients with COVID-19 Infection

Three types of non-invasive ventilatory support are considered in patients with COVID-19 disease: High Flow Nasal Oxygen (HFNO), Continuous Positive Airway Pressure (CPAP) and Non-Invasive Ventilation (NIV).

**High Flow Nasal Oxygen (HFNO)**

High-flow nasal oxygen (HFNO) therapy is an oxygen supply system capable of delivering up to 100% humidified and heated oxygen at a flow rate of up to 60 L/min. In a small study of all-cause hypoxic respiratory failure, high-flow oxygen therapy had a significant improvement in 90-day mortality compared to either non-invasive ventilation or standard oxygen therapy but was not associated with a reduced need for intubation in severe hypoxic respiratory failure\(^{18}\). Over recent years, HFNO has become a standard part of the management of hypoxic respiratory failure. Its utility in the management of COVID-related respiratory failure is unproven.

There are several considerations with the use of HFNO in the management of COVID-19 disease:

- Local maximum oxygen delivery flow rates may limit the number of patients that can receive the intervention and this therapy may place a significant burden on local oxygen supplies.
- HFNO is classified as an AGP and should be carried out in an appropriate setting using enhanced PPE.

Ongoing hypoxia, deteriorating gas exchange and increasing work of breathing in patients managed with high flow nasal oxygen should trigger review and consideration of the need for intubation and invasive ventilation if deemed appropriate.

**Continuous Positive Airway Pressure (CPAP)**

CPAP is a form of non-invasive positive pressure ventilation through which a constant level of pressure above atmospheric pressure is applied to the airways via an interface, which is most often a facemask or helmet hood. Evolving experience and low quality evidence suggests that a proportion of patients with COVID-19 disease have CPAP-responsive hypoxia\(^{19}\), and increasingly CPAP has been used as the non-invasive respiratory support of choice in COVID-19 disease. CPAP therapy is usually “oxygen neutral” with regard to provision but oxygen provision and capacity across and within hospital sites is an important consideration. CPAP should be delivered in a fully monitored environment with trained staff who are vigilant to patient deterioration. CPAP is classified as an AGP and should be carried out in an appropriate setting using enhanced PPE.

Further guidance on the use of [CPAP for patients with COVID-19 related respiratory failure](#) is available.
Bilevel Positive Airway Pressure (BiPAP)

Bilevel Positive Airway Pressure [BiPAP], (also called Non-Invasive Ventilation (NIV)) in COVID-19 should only be offered for standard indications e.g. to patients with underlying lung disease for treatment of type 2 respiratory failure. NIV is classified as an AGP and should be carried out in an appropriate setting using enhanced PPE.

4.2.3 Tracheal Intubation in Critically Ill Patients with COVID-19 Infection

Some patients with COVID disease will require intubation to facilitate invasive ventilation for hypoxia or worsening respiratory failure. Tracheal intubation is recognised to be a high risk procedure in critically ill patients. Hypotension and desaturation are common unintended consequences (around 20% of all critically ill patients)\(^2\). In addition, the first attempt success rate of intubation in critically ill adults is significantly less than in elective settings\(^2\).

Key considerations to improve patient and staff safety during tracheal intubation of a patient with SARS-CoV-2 infection are summarised below:

- Tracheal intubation is an AGP and is high risk to the intubator and other staff involved. All staff should wear enhanced PPE. Wherever possible, the staff present should be limited to the minimum required for safe intubation (one intubator, one airway assistant, one to administer drugs and to monitor patient physiology). A runner in full PPE should remain outside the room in case of the need for help or further equipment.

- Wherever possible, intubation should take place in a negative pressure environment or side room with a high number of air exchanges.

- The development and/or use of COVID specific checklists/cognitive aids for tracheal intubation to aid communication and plan/respond to difficulty is strongly recommended.

- Simulation of complex scenarios, drills and skills can be useful for team education through experiential learning, and can also contribute to the optimisation of systems processes.

- Airway management should be performed by the most experienced available operator, so as to maximise the success of first-pass intubation.

- Consideration should be given, dependent on the experience of the intubator, to the use of airway techniques which may improve first pass success (including use of video laryngoscopy or other airway adjuncts such as gum elastic bougies or stylets).

- Patients with COVID-19 pneumonia are often grossly hypoxic. In order to minimise desaturation during intubation attempts, wherever possible patients should be pre-oxygenated for a period of 5 minutes in order to denitrogenate the functional residual capacity and to provide an oxygen store.

- A rapid sequence technique is appropriate for induction of a critically ill patient. Wherever possible, to avoid aerosol generation, mask ventilation should be avoided;
however in this hypoxaemic patient group it is often necessary, and the decision whether or not to use mask ventilation should be made by the lead intubator on a case by case basis. If required for oxygenation during induction, a two-person, two-handed technique is advocated.

- Consideration should be given to the need to clamp endotracheal tubes during connection and changes of breathing circuits as this may reduce the risk of contamination of the clinical environment with aerosolised particles.

- Caution should be used around the time of extubation in patients with COVID-19 disease. Patients in this group have been reported to have a higher than expected rate of extubation failure, with increased rates of airway swelling and stridor reported21.

- The use of adjunctive "intubation boxes" as an attempt to reduce aerosol generation may actually increase aerosol generation and should not be used for intubation of critically ill patients with COVID-19 disease22.

### 4.2.4 Invasive Ventilation in patients with COVID-19 pneumonitis

**Ventilator Strategy**

Lung protective ventilation is the cornerstone of supportive, evidenced-based care in patients who fulfil the Berlin definition for ARDS23:

- Tidal volumes should be kept to <6ml/kg of predicted body weight. Predicted body weight (in kilograms) can be calculated in men as 50 + (0.91 × [height in centimetres − 152.4]) and in women as 45.5 + (0.91 × [height in centimetres − 152.4]). Surrogate measures for predicted body weight, such as the olecranon-ulnar distance chart can also be used.

- Plateau pressures higher than 30 cmH$_2$O should be avoided, and should be kept < 26 cmH$_2$O where possible. Ideally, the driving pressure (plateau pressure – PEEP) should be kept less than 15 cmH$_2$O.

- In the early phase of the illness, patients may have preserved compliance and may have a poor response to increasing PEEP. An initial PEEP of 10 cmH$_2$O will often suffice but should be titrated up or down depending on the clinical response and FiO$_2$. A higher PEEP strategy is suggested for patients with moderate to severe ARDS and poor compliance.

- There is no evidence to support inverse ratio ventilation in patients with COVID-19 pneumonia.

**Neuromuscular Blockade**

Neuromuscular blockade should be considered for patients with moderate to severe ARDS with P:F ratio of < 20 kPa24. In addition, neuromuscular blockade could be considered for patients with high transpulmonary pressures and a high spontaneous minute ventilation, to
reduce the burden of patient self-inflicted lung injury. The use of neuromuscular blockade must be balanced against the risk of critical illness polyneuropathy and myopathy, prolonged ileus and the potential for awareness in this patient group.

**Prone Ventilation**

Prone Ventilation is an evidence based intervention for patients with ARDS and a P:F ratio < 20kPa on FIO2 > 0.6\(^{16}\). There is growing European and UK consensus that patients with COVID-19 disease respond well to proning\(^{25}\). Patients should be left in the prone position for a minimum of 16 hours, and patients may require multiple episodes of proning over several days. Close attention should be paid to eye care, pressure care, and line sites in patients nursed in the prone position. If many patients require proning concurrently, the development of a dedicated “proning-team” to co-ordinate multiple position changes may be beneficial.

### 4.2.5 Extracorporeal Membrane Oxygenation

Patients who are failing to improve with conventional care should be considered for referral for veno-venous extracorporeal membrane oxygenation (ECMO) therapy through the ECMO National Referral Pathway\(^{26}\), if they meet the following inclusion criteria:

- Potentially reversible severe respiratory failure
- Lung Injury (RESP) score ≥3 or uncompensated hypercapnia with a pH 7.20 or less
- Failed trial of Ventilation in the prone position > 6 hours
- Failed optimal respiratory management / lung protective ventilation
- Clinical Frailty Score of ≤ 3

If the patient RESP score is ≤ 3 then ECMO will only be considered if there is consensus agreement between more than 2 ECMO centres.

The [ECMO National Referral Pathway](#) can be accessed via Signpost.

Care for patients with COVID-19 disease who require ECMO is provided through one of 6 regional ECMO centres. For patients in Scotland this would normally be at the ECMO centre at Aberdeen Royal Infirmary. Provisional outcome data for the European cohort of patients requiring ECMO support in COVID-19 disease indicates a survival rate of 78%\(^{27}\).

### 4.3 Fluid Management and Renal Replacement Therapy (RRT)

At the time of presentation to hospital with COVID-19 disease symptoms, patients are often 7-14 days into their illness course and may be dehydrated at the point of presentation. On admission to hospital all patients require a careful fluid assessment and may need a degree of judicious fluid resuscitation. In the early stages of admission to hospital it is often helpful to avoid an excessively positive fluid balance, rather than targeting a negative fluid balance.
Beyond the resuscitation phase of illness, a negative fluid balance is normally targeted in patients with ARDS. A conservative fluid strategy has been shown to improve oxygenation and increase the number of ventilator-free days\(^2^8\). This is normally achieved with diuretic therapy but on some occasions, it is necessary to institute renal replacement therapy to achieve a negative fluid balance. Electrolytes such as sodium, potassium, magnesium and phosphate should be kept within the normal range.

Classical indications for initiation of renal replacement therapy (RRT) include hyperkalaemia, refractory acidosis, uraemia and fluid overload. In patients with COVID-19 and AKI, RRT may be initiated to achieve a negative fluid strategy.

There is anecdotal evidence that patients undergoing RRT with COVID-19 disease are experiencing a greater frequency of filter thrombosis than the general ICU population despite the use of recognised methods of anticoagulation in the filter circuit. Consideration should be given to using a continuous systemic infusion of unfractionated heparin (UFH), instead of citrate and/or low molecular weight heparin (LMWH), for anticoagulation in patients with COVID-19 disease who are receiving renal replacement therapy\(^2^9\).

In those patients receiving UFH for prevention of filter thrombosis, anti-Xa measurements are a more reliable measure of the effectiveness of UFH than APTTr (which is often falsely increased or reduced in this patient group owing to the presence of very high Factor VIII levels or lupus anticoagulant)\(^2^9\).

Additionally, please refer to the guidance on prevention of circuit thrombosis in adult inpatients who are COVID-19 positive and undergoing RRT on critical care wards.

### 4.4 Pharmacological Treatments in COVID-19 Infection

The mainstay of management in critically ill patients with COVID-19 disease is supportive care. A number of pharmacological interventions have an evolving evidence base. There is ongoing research in this area.

#### 4.4.1 Steroid Therapy

Corticosteroids, and in particular dexamethasone and hydrocortisone, have an indication in the management of patients with COVID-19. Following recent publication of the REMAP-CAP trial for hydrocortisone and a meta-analysis of corticosteroids, the World Health Organization (WHO) has recently issued new interim guidance recommending the use of systemic corticosteroids in severe and critical COVID-19 disease.

The WHO guidance makes two recommendations:

1. strong recommendation for systemic (intravenous or oral) corticosteroid therapy in patients with severe and critical COVID-19, and
2. a conditional recommendation not to use corticosteroid therapy in patients with non-severe COVID-19.
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In the UK this would apply to hospitalised patients receiving supplemental oxygen.

The MHRA have issued guidance on the use of corticosteroids through the Central Alerting System.

Dexamethasone or hydrocortisone should be offered to people with severe or critical COVID-19 (in line with updated WHO guidance); that is, people with any of the following:

- acute respiratory distress syndrome (ARDS)
- sepsis or septic shock
- other conditions that would normally need life-sustaining therapies such as ventilation or vasopressor therapy
- signs of severe respiratory distress
- oxygen saturation <90% (or deteriorating) on room air
- increased respiratory rate (>30 breaths per minute in adults and children over 5 years).

Corticosteroids should not be used in non-critical COVID-19 disease.

For dexamethasone the recommended adult dose schedule (as applied from the WHO guidance) is:

- For dexamethasone 2mg tablets: dosage three tablets once a day for 7-10 days
- For dexamethasone 2mg/5mL oral solution: dosage 15mL once a day for 7-10 days
- For dexamethasone 3.3mg/mL intravenous 1ml ampoules: dosage 1.8mL (5.94mg) once a day for 7-10 days

Treatment should stop if the patient is discharged from hospital within 10 days.

For patients able to swallow and in whom there are no significant concerns about enteral absorption, tablets should be prescribed. IV administration should only be used where tablets or oral solution are not appropriate, or not available.

When prescribing dexamethasone consideration needs to be given to the gastric ulcer protection effect of proton pump inhibitors according to local hospital policy.

For hydrocortisone the recommended adult dose schedule (as applied from the WHO guidance) is:

- 50mg hydrocortisone administered intravenously three times per day for 7-10 days
- A longer low dose duration can be considered for patients with septic shock
4.4.2 Remdesivir

Remdesivir is an adenosine analogue and RNA dependent-polymerase inhibitor, which blocks viral replication. The ACTT-1 trial preliminary results demonstrated that the use of remdesivir for up to 10 days was associated with a shorter time to clinical recovery vs placebo. The benefit was most pronounced for patients early in the course of their disease who were requiring supplementary oxygen therapy. However, the trial did not provide any evidence of benefit for patients requiring advanced respiratory support, including HFNO, NIV or invasive ventilation. The benefit for remdesivir in critically ill patients is therefore uncertain.

Remdesivir is approved for use in the UK through an interim clinical commissioning policy.

Supplies in NHS Scotland are being organised via Health Improvement Scotland and NSS National Procurement.

**Eligibility Criteria:**

- Hospitalised with coronavirus disease 2019 (COVID-19)
- Pneumonia requiring supplemental oxygen
- Adults, and adolescents ≥ 12 years of age and ≥ 40 kg
- eGFR ≥ 30ml/min
- Alanine Aminotransferase (ALT) below 5 times the upper limit of normal at baseline

**Additional criteria:**

In times of limited supply, two additional criteria will be necessary in order to allocate remdesivir to those with the greatest capacity to benefit (patients in the earlier stages of respiratory failure). In this context the following criteria must also be met:

- At the time of decision to treat with remdesivir patients should not be receiving ongoing mechanical ventilation or ECMO. Patients who present with an initial rapid deterioration can, however, be considered for treatment with remdesivir.
- Multi-disciplinary team assessment should determine if patients not suitable for escalation would benefit from initiation of treatment with remdesivir.
- If patients on remdesivir require escalation, continuation of the drug should be considered by multi-disciplinary team assessment.

Dexamethasone can be administered alongside remdesivir. Currently there is no trial data to confirm the combination has additional benefits.

**Dosing Schedule:**

In patients fulfilling the access criteria for Remdesivir, the dosing schedule is detailed below:

- 200mg on day one, followed by 100mg daily for a further:
o Nine days in patients requiring invasive ventilation and/or ECMO
o Four days in those NOT requiring invasive Ventilation and/or ECMO. In these patients up to an additional 5 days treatment (i.e. a total of ten days of treatment) can be considered if the patient does not demonstrate clinical improvement, following further specialist discussion

Daily measurement of Urea and Electrolytes (U&Es) and liver function tests (LFTs) are required in patients being treated with remdesivir, and the treatment should be discontinued in patients in whom the renal function or liver function tests deteriorate.

4.4.2 Antimicrobial Therapy

Routine antibiotics are not recommended for uncomplicated COVID-19 disease. Antibiotics should be considered if there is suspected super-added bacterial infection. Many patients will be commenced on antibiotics at presentation to cover for atypical community-acquired pneumonia. The need for antibiotics should be reviewed daily and in the absence of positive cultures should be discontinued. Microbiologist involvement in the multi-disciplinary care of critically ill patients is recommended.

For further guidance on use of antimicrobial management and antibiotic stewardship in the setting of COVID-19 disease, refer to the Scottish Antimicrobial Prescribing Group guidelines on COVID-19.

In order to reduce the burden of healthcare associated infection, particularly whilst staff work cohorted areas in enhanced PPE, close attention and vigilance should be paid to strict interpatient infection control measures, daily review of line sites, and completion of ventilator associated pneumonia (VAP) prevention bundles.

4.4.4 Thromboprophylaxis

There is increasing recognition that patients with COVID-19 have higher rates of thromboembolic events, particularly pulmonary thromboembolism. All inpatients with confirmed or suspected COVID-19, should receive thromboprophylaxis during their admission, as long as no contra-indications are present. In critical care settings, an increased, intermediate-dose of thromboprophylaxis, in keeping with developed local protocols, should be considered to reduce the risk of venous thromboembolism.

Full guidance on the prevention and management of thromboembolism in hospitalised patients with COVID-19-related disease is provided here.
References


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This guideline was reviewed by the Scottish Government COVID-19 Clinical Cell.