Guidelines for the Management of COVID-19 in the Intensive Care Unit

Prince of Wales Hospital

Version 3.4, 1 September 2021

These instructions are intended as a guide only. They are not exhaustive and exist in addition to standard ICU care. They describe initial settings for patients admitted to the ICU primarily for treatment of COVID-19. The guidelines have been agreed upon by the consultant group. Deviation from these guidelines should be discussed with intensivist on-call. This guidance was appropriate at the time publication, changes in the pandemic and evidence base over time may render some elements obsolete.

REFERRALS & CODE BLUE

Refer to the Escalation Pathway for COVID-19

- All COVID patients should ideally have a Resuscitation Plan & suitability for ICU & intubation assessed by the home team on admission to hospital
- Where possible, there will be daily communication between DB4 and ICU regarding each other's bed state and patient cohort
- Patients referred to ICU must have been discussed with a senior member (Advanced Trainee of higher) of the referring team *prior* to referral to ICU
- **All COVID admissions should be discussed with the intensivist on-call *before* accepting the referral**

Admission to HDU/ICU

- Patients that meet the threshold for **referral** to ICU on the Escalation Pathway for COVID-19 will not *necessarily* need to be admitted to the HDU/ICU
- Patients that meet the threshold for **consideration for intubation** per the Escalation Pathway should be admitted to the HDU/ICU unless this is otherwise contraindicated
- The criteria for HDU/ICU admission for **non-COVID indications** in patients with COVID-19 are unchanged from standard practice

Staff Exposure

When attending a **referral or Code Blue** for a known or suspected COVID-19 patient effort should be made to limit staff exposure

- Unvaccinated staff should avoid exposure wherever possible
- Always don appropriate Airborne Precautions PPE, **this is mandatory even if it may delay resuscitation**
- The attending ward team should continue BLS whilst the ICU team don PPE
- Minimise numbers in the room
- Only repeat examination where clinically indicated (i.e. it is not necessary for ICU staff to repeat exam if has been recently completed by referring team)
- Where possible move the patient to a designated single room, otherwise evacuate other patients and visitors from the area
- Intubation, supraglottic airways and airway suctioning are considered aerosol generating procedures (AGP)
- It is unclear if compressions is an AGP
- Defibrillation and face mask oxygen is not considered an AGP

INFECTION CONTROL FOR PATIENTS WITH "UNKNOWN" COVID STATUS

- The decision for infection control measures for COVID-19 lies with Infectious Diseases consultant on for the day
- There are 3 elements that inform the decision for infection control status:
    - Clinical presentation, including likely non-COVID diagnoses
    - Exposure history using the screening tool
    - Swab results
- Where a patient is unable to provide the admitting history this must be sought through NOK/family/etc. to provide an appropriate risk assessment. This should ideally **be done prior to admission to ICU**
- Swabs, rapid or not, do not necessarily 'clear' a patient as they may be within the incubation period. The likelihood of this is determined by clinical presentation & exposure history.
- Where a patient must be admitted to ICU and their COVID status remains unknown they are to be admitted to the **non-COVID ICU into a side room with airborne precautions**. Ideally this would be bedspace 13 with adjacent anteroom used for donning & doffing.

AIRWAY

See Escalation Pathway for COVID-19

- Mechanical ventilation is associated with increased mortality in COVID-19.
- Whenever possible a discussion with the admitting consultant and intensivist on-call should occur ***before*** intubation.
- The decision to intubate will be influenced by prognostic risk factors, biomarkers and functional background.
- The ROX Index can be used to predict intubation for patients with COVID-19 using HFNP: mdcalc.com/rox-index-intubation-hfnc

Indications for Intubation

Intubation should be **CONSIDERED** for COVID-19 when:

- FiO2 >40% or >6L via HM for SaO2 92% or P:F <300
- RR >30 or Respiratory Distress
- Sepsis or new organ failure
- Drop in GCS by >2 points

Intubation **IS LIKELY** for COVID-19 when:

- FiO2 >60% or 10L/min via HM for SaO2 92%
- ARDS or P:F <200
- Ongoing deterioration despite HFNP/NIV/Prone position
- Shock

Intubation for **non-COVID indications** in COVID-19 patients, such as coma or airway concerns, remains unchanged

Intubation per Safe Airway Society guidelines

Use dedicated COVID Intubation Team where possible (per their own guidelines)

Extubation

- HFNP and NIV potentially increase risk to staff and necessitates use of isolation room. Where possible avoid extubation to these devices.
- Coughing and respiratory distress at extubation are high-risk aerosol generating procedures
- Duration of intubation tends to be 1-2 weeks. Prolonged intubation may result is airway swelling which should be assessed prior to extubation

Tracheostomy

- Tracheostomy is an AGP that exposes multiple staff members although this appears to be ameliorated with appropriate PPE
- The risks & benefits of tracheostomy should be considered only after 10 days of mechanical ventilation (ANZICS)

RESPIRATORY

- CXR Day 0 and then only as clinically indicated
- Target SaO2 90-92%
    - SaO2 88-92% for COPD
    - SaO2 94-96% for pregnant, cardiac or cerebral ischaemia
- Avoid the use of nebulisers (use MDI with spacer for non-intubated patient)
- Be aware that expiratory viral filters can become saturated when using inhaled medications and lead to ventilator failure (obstructed expiratory airflow, delay return to PEEP at end of inspiration)

High Flow Nasal Prongs

- High Flow Nasal Oxygen may reduce the need for intubation and is suitable for patients that require ICU/HDU for observation with FiO2 >40% or 6L/min via HM but not yet indicated for mechanical ventilation (National Taskforce)
- Where possible HFNP should be delivered in a negative-pressure or isolation room and ensure contact, droplet and airborne precautions are in place. (Per National Taskforce)

Non-Invasive Ventilation

- NIV may be used for patients with COVID-19 for a **standard non-COVID indication** such as:
    - COPD
    - Pulmonary oedema
    - OSA
- Use of NIV for COVID patients **must** be discussed with the consultant
- Where possible NIV should be delivered in a negative-pressure or isolation room and ensure contact, droplet and airborne precautions are in place. (Per National Taskforce)
- The use of NIV in a COVID-19 patient does *not* necessarily require admission to ICU

- Continuous positive airway pressure (CPAP) NIV may have a **limited** role in management of COIVD-19, such as for those patients considered not suitable for intubation
- Bilevel positive airway pressure (BiPAP) NIV is **unlikely** to be of benefit over CPAP for COVID-19 and carries risks such as patient self-inflicted lung injury (P-SILI)

Awake Prone Positioining

The prone position should be considered for all non-intubated patients in the ICU/HDU that require supplemental oxygen using the following protocol:

- 30 minutes to 2 hours lying fully prone (bed flat)
- 30 minutes to 2 hours lying on right side (bed flat)
- 30 minutes to 2 hours sitting up (30-60 degrees) by adjusting head of the bed
- 30 minutes to 2 hours lying on left side (bed flat)
- 30 minutes to 2 hours lying prone again
- Continue to repeat the cycle.....

From Intensive Care Society (UK) "ICS Guidance for Prone Positioning of the Conscious COVID Patient 2020"

Sedation should not be used to achieve prone positioning for patients that are non-compliant

Initial Ventilator Settings

- Use volume-targeted pressure-regulated mode
    - (On our Hamilton ventilators the mode is APVsimv or SIMV+)
- Target Vt for 6mL/kg (use ideal body weight, establish patient's height with tape measure)
- Pplateau <30cmH2O
- Respiratory rate for pCO2 that achieves pH >7.20
- Inspiratory time >1.3 secs (I:E 1:1.5 or closer to 1:1)
- Nursed in semi-prone position, 2 hours per side
- PEEP: Start 12cmH2O, increase to 15 if haemodynamically stable, then per FiO2 according to ARDSnet High PEEP table (below, available on Google, use lowest setting per FiO2)

Higher PEEP/lower FiO2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

Subsequent Ventilator Settings

Two phenotypes of respiratory failure have been postulated for COVID-19. Subsequent ventilation management can be tailored to the phenotype.

i) *Predominantly Hypoxic* with “normal” compliance (L-type)
- higher compliance (e.g. >30mL/cmH2O), lower driving pressure (e.g. <15cmH2O)
- consider lower PEEP (10cmH2O)
- less likely to be responsive to recruitment manoeuvres

ii) *More classic ARDS* (H-type)
- poor compliance (e.g. <30mL/cmH2O), higher driving pressures
- maintain higher PEEP per ARDSnet table (above)

Neuromuscular Blockade

- Routine use of NMB’s is not recommended
- Paralysis may be indicated for refractory hypercarbia, dysynchrony, poor compliance or progressive hypoxia (P:F <150)
- Bolus first then cistracurium infusion, target TOF 2/4

Recruitment Manoeuveres

- Recruitment manoeuvres should not be used routinely
- They may be beneficial on an 'as indicated' basis for recruitment during acute hypoxia
- Avoid high pressure (>60cmH2O) staircase manoeuvres

Refractory Hypoxaemia

- PE is reported in up to 25% of patients with severe COVID-19 (FICM/ICS UK)
- For ARDS induced hypoxaemia:

If P:F ratio persistently <150:
Prone position for 12-16 hours per day
Continue or restart **paralysis** with cisatracurium infusion

If P:F ratio STILL remains <150:
Start inhaled prostacyclin (preferred due for anticoagulant effect) or inhaled nitric oxide ***AND*** consider suitability for ECMO

ECMO

- ECMO may be indicated if SaO2 <88% after 12 hours prone ventilation on FiO2 >80% or hypercapnic failure with pH <7.20
- To maintain state resources the decision to start a COVID patient on ECMO should be discussed with on-call specialist centre (RPA or SVH, roster at https://www.nsw-ecmo.net/) (per NSW Health & ACI)

DISEASE MODIFYING AGENTS

- The use of any disease modifying agents should be discussed with ID
- Consult the National COVID-19 Clinical Evidence Taskforce for the most up to date recommendations
- Any therapeutics not recommended by the above Taskforce should only be used in the context of a clinical trial
- Prince of Wales can enrol patients into the REMAP-CAP study of COVID therapeutic agents
    - Study drugs for REMAP-CAP should be clearly described as “Study” or “Trial” drugs on eRIC or eMEDS
- As of 7 July 2021 the recommended Disease Modifying Agents per the Taskforce are:

- Dexamethasone (Steroid)
    - For any patient requiring supplemental oxygen, including ventilation
    - 6mg IV daily for 10 days
- Remdesivir (Antiviral)
    - For patients requiring oxygen but not yet ventilation (NIV or IMV)
    - Should **not** be started for those on ventilation however, may be **continued** for those who require ventilation whilst already on a course of Remdesivir
    - 200mg IV on first dose then 100mg IV daily for 5 days

- Tocilizumab (IL-6 inhibitor) (or Sarilumab)
    - For those on oxygen with signs of inflammation (CRP >75)
    - May have additive effect with steroid
    - Weight-based single dose (can be repeated once), IV q60mins
        - >90kg 800mg
        - 66-90kg 600mg
        - 41-65kg 400mg
        - <40kg 8mg/kg
    - Sarilumab is alternative IL-6 inhibitor
- Baricitinib (JAK inhibitor)
    - UpToDate suggests using either IL-6 inhibitor *OR* Baricitinib, not both
    - For those requiring oxygen or ventilation
    - 4mg PO for 14 days
- Casirivimab plus Imdevimab (REGEN-COV)
    - Only in the seronegative patients (no detectable COVID antibodies, not vaccinated)
    - Not currently available in Australia

CARDIOVASCULAR

- Patients with significant inflammation may be unexpectedly hypovolaemic at presentation
- Hypovolaemic hypotension & shock has been reported complication at intubation and with institution of higher airway pressures
- The above is exacerbated by early institution of diuretic therapy

- Dynamic measures of fluid responsiveness (straight-leg raise, fluid challenge, EV1000) should be used to guide fluid resuscitation
- Plasmalyte-148 is preferred resuscitation fluid
- After 24 hours of haemodynamic stability a conservative fluid strategy should be instituted targeting a neutral fluid balance
- Target MAP 65 (70 if significant history of hypertension)
- Bundle line insertion to reduce staff exposure
- Cardiac dysfunction, of any cause, has been reported in up to 33% of COVID-19 ICU patients
- Viral myocarditis 10-15 days after onset is reported but uncommon (FICM/ICS UK)
- ACE-I & ARB's can be continued if indicated

NEUROLOGICAL

- UK experience suggests 1% incidence of CVA and 0.5% seizure (FICM/ICS UK)
- Acute Disseminated Encephalomyelitis (ADEM) is described in severe COVID-19
    - Diagnosis by MRI
    - Treatment = Methylprednisolone +/- IVIg
- COVID-related GBS has been reported

GASTROINTESTINAL

- NGT at intubation
- Insulin resistance is common in COVID-19 and may require intensified glycaemic control (FICM/ICS UK), particularly when being treated with Dexamethasone
- Generally standard care
- Consider hypocaloric feeding, i.e. 20mL/h usual NG feed, unless signs of malnutrition, for 3-7 days for ARDS
- LFT's are often elevated in COVID-19, no specific therapy recommended (FCIM/ICS UK)

RENAL

- AKI is common in COVID-19 and associated with poorer outcomes
- General approach is to target euvolaemia
- Use targeted fluid resuscitation (see Cardiovascular section) and avoid routine use 'maintenance fluids'
- Standard approach to management of AKI and use of RRT

HAEMATOLOGICAL

- Hypercoagulability appears to be a feature of severe COVID-19
- Daily bloods should include Coags, Fibrinogen, Trop, Ferritin & LDH
- Characterised by:
    - APTT/INR normal or mildly raised
    - Platelets normal or mildly raised
    - Fibrinogen elevated
    - D-dimer elevated

    - Also elevated FVIII & vWF
    - ROTEM shows decreased CT, CFT (A5) & LY30, increased MCF
- Distinct from DIC
    - More clotting with COVID
    - More bleeding with DIC
- Presents with more commonly with venous than arterial thrombus
    - VTE incidence up to 33% (despite prophylactic anticoagulation)
    - PE incidence 7-25% (despite prophylactic anticoagulation)
    - MI 9%
    - CVA 1%
- Despite studies there is no evidence to support use of increased anticoagulation
- Recommended VTE/PE **prophylaxis** is **Enoxaparin 40mg SC daily** (per National Taskforce)
- Follow standard management for suspected or confirmed thrombus
    - DVT USS as indicated
    - CTPA as indicated
    - Therapeutic Enoxaparin or IV Heparin at standard doses for usual indications (i.e. confirmed PE/DVT)
- Clotting in vascular devices or extracorporeal circuits can be considered indication for therapeutic anticoagulation (per UpToDate)

INFECTION

- Differentials should be excluded on admission (if not already done so)
    - Standard resp viral panel
    - Atypical screen (legionella, mycoplasma, pneumococcal)
    - Sputum/NBL
    - BC, MSU
- CRP & PCT daily

- Empiric CAP or HAP until COVID confirmed
- Ongoing antibiotics are not recommended for confirmed COVID without evidence of superinfection (check PCT)
- Consider bacterial or <u>fungal</u> (reported higher rates) super-infection is case of secondary deterioration
- There are reports of reactivation of TB, CMV, HSV & VZV after COVID treatment with steroids and IL-6 inhibitors

COVID DURING PREGNANCY

- Pregnancy does not appear to increase risk of contracting COVID-19 (UpToDate)
- Pregnant women are 2-3x more likely to deteriorate and die from COVID than age-matched non-pregnant women
- However risks are still relatively low when compared to other COVID risk factors. The risks for pregnancy are (UpToDate, n>80,000):
    - Risk of death 0.1 - 1.5%
    - Risk of Intubation 1.6-2.9%
    - Risk of ICU 3.3 – 13%
- Specific risk factors during pregnancy are: Age >35, BMI >25, DM, HT (RCOG UK)
- There does not appear to be any increased obstetric risk beyond an increase in iatrogenic pre-term birth
- There are normal changes in respiratory physiology during pregnancy that are relevant to assessing a patient with COVID-19
    - Minute ventilation is increased, this will limit the ability of standard nasal prongs to provide a steady FiO2, **HFNO** will be a more reliable option
    - Decreased FRC, diaphragmatic excursion and chest wall compliance predispose to lung collapse, particularly during extended bed rest. These may result in oxygenation defect beyond COVID pneumonia. These may be amenable to positive pressure ventilation (**NIV**)
        - NIV can predispose to vomiting during pregnancy. Prophylactic **anti-emetics** are recommended.
    - Normal paCO2 is lower in pregnancy (~32mmHg). However, there is no evidence of maternal or foetal injury with permissive hypercapnia allowing paCO2 as high as 50mmHg
    - Particular attention should be paid to **pH during relative hypercarbia**, acidosis may detrimentally affect foetal oxygenation saturation
    - Increased 2,3-DPG during pregnancy may make it more difficult to saturate haemoglobin at the same paO2. **Higher FiO2** may be required.
    - Normal systolic blood pressure may be as low as 90mmHg

- In order to maintain foetal oxygenation the **target for pregnant women is SaO2 ≥95%**
    - A paO2 >70mmHg maintains a favourable oxygen gradient to the placenta (UpToDate)
- Given the higher SaO2 targets, and relative difficulty in saturating haemoglobin, pregnant women would be expected to require a higher degree of oxygenation support for the same level of COVID-induced lung disease. The **P:F ratio** can provide an objective measure of oxygenation capacity.
- Pregnant patients with COVID should have multi-disciplinary involvement from their admitting team, O&G +/- ICU.
    - Birthing plans and foetal monitoring should be discussed with the O&G/Maternal-Foetal medicine team.
- The thresholds for escalation to ICU discussion are as for the non-pregnant patient
- Beyond the considerations above for HFNO & NIV there are no specific differences to the respiratory management (National Taskforce)
- The current (19 August 2021) recommendations for disease modifying agents in non-pregnant patients can all be used in pregnancy, except Baricitinib, with the following considerations:
    - Prednisone 40mg is preferred over dexamethasone due to potential foetal effects.
        - Attention should be paid to BSL's, hyperglycaemia may represent steroid-induced hyperglycaemia or gestational diabetes
    - Tocilizumab may be preferentially used earlier, including before Remdesivir
    - Remdesivir less promoted
    - Barcitinib is **only currently recommended in a research context**
- The recommended DVT prophylaxis is **enoxaparin 40mg SC daily** (per non-pregnant adult)
- There are a number of complications of pregnancy that are relevant during care for COVID:
    - Non-specifically raised LFT's may represent HELP
    - There is an increased risk of pre-eclampsia during COVID-19
    - There is increased risk DVT/PE both during pregnancy and COVID however, the D-dimer is normally elevated in both conditions rendering it unhelpful in making the diagnosis. A high index of clinical suspicion should be maintained.
    - Peri-partum cardiomyopathy may present with signs similar to sepsis
- Prone positioning is possible during pregnancy (Tolcher *et al.*, 2020)
    - Guide is located here: https://cdn-links.lww.com/permalink/aog/b/aog_136_2_2020_06_02_tolcher_20-1208_sdc1.pdf
    - Video for non-intubated is here: https://www.youtube.com/watch?v=7orutHYuXFQ
    - Video for intubated is here: https://www.youtube.com/watch?v=SOgwakxeyXE

Escalation Pathway for COVID-19

Prince of Wales Hospital ICU. Version 2.3, 1 September 2021

	HYPOXIA only	SEPSIS
IDENTIFICATION of Risk Factors at Admission		
	All patients admitted for COVID should have resuscitation and intubation status discussed and documented	
	Age >50, particularly >70 **Co-morbidities:** CVD, HT, DM, chronic lung disease, CKD, cancer, immunosuppression **Inflammatory markers:** CRP >75, D-dimer >1, raised ferritin, raised top/BNP, leukopaenia **Time course:** deterioration <1 week form onset, rapid rate of progression *Consider deterioration prediction tests: 4C & ROX*	
RECOGNITION of deterioration		
	Sustained FiO2 ≥6L/min via HM or FiO2 ≥40% for SaO2 ≥92%	RR >30 Respiratory distress Relative Hypercapnia SBP <100 New Organ failure Drop in GCS >2 points
	DISCUSS WITH AMO +/- ICU ***RE: Management & Admission to ICU***	
OBSERVATION on Ward, HDU or ICU		
	Location of higher level of observation will depend on: • *ICU & ward expected capacity* • *Identified risk factors for deterioration* • *Discussion between admitting consultant and ICU*	
MANAGEMENT		
	Continuous SaO2 monitoring HFNP if single room and appropriate PPE available, otherwise O2 via HM Awake prone positioning IDC and neutral fluid balance Disease modifying agents (e.g. Dexamethasone), if not already started	
INTUBATION consideration, **Transfer to HDU/ICU**		
	Requiring FiO2 >60% or HM >10L/min for SaO2 92% ARDS or P:F < 200 Ongoing deterioration despite HFNP / NIV / Prone	Septic shock: qSOFA ≥ 2/3 SBP <90 Lactate >2.5

This guide will not cover all eventualities. If in doubt call senior or ICU for advice.

Deterioration Prediction Scores

1. The 4C Mortality & Deterioration risk prediction score: isaric4c.net/risk
2. The ROX Index for risk of intubation after HFNP: mdcalc.com/rox-index-intubation-hfnc

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