

Evidence-based COVID-19 ICU Management Guide v2.0

Aims of Management Guide

COVID-19 patients admitted to ICU respond to good quality supportive care. This evidence-based guide aims to highlight unique features of COVID-19 management including:

- Monitoring for secondary complications associated with COVID-19 infection
- Differences in approach to common ICU issues to prevent unnecessary interventions which may put patient and staff at risk

Monitoring for Secondary Complications of COVID-19

Four major complications associated with COVID-19 have been highlighted from the literature:

- 1. COVID-19 Associated Coagulopathy (CAC)
- 2. Cytokine Storm/Secondary HLH/Macrophage Activation Syndrome
- 3. Secondary Bacterial Superinfection
- **4. Viral Myocarditis** *(may be seen as part of cytokine storm)

Laboratory Investigations on Admission

- CBC, Urea, Creat, Extended Lytes (Mg²⁺/PO₄/iCa²⁺), D-Dimer, LFTs (AST, ALT, GGT, ALP, Direct and Total Bili, Alb, LDH), Ferritin, Coagulation Screen (INR/PTT), Fibrinogen, Troponin, Procalcitonin, CRP
- Blood Cultures x 2
- NP Swab for Viral PCR (if not already sent) for all patients

AND

• Tracheal aspirates for Viral PCR (if not already sent) for intubated patients

Daily Bloodwork

• CBC, Urea, Creat, Extended Lytes, Coagulation Screen, Fibrinogen

Monday/Wednesday/Friday

- LFTs, (AST, ALT, GGT, ALP, Direct and Total Bili, Alb, LDH), Ferritin, D-Dimer, CRP
- Lipid Profile (LDL, HDL, Triglycerides) if ferritin >2000ng/mL in addition to daily orders
- · Reassess frequency of these additional tests after Week One

If increasing leukocytosis (WCC >10x10 9 /L), clinical concern for bacterial infection AND Temp >38.5 $^\circ$ C

Procalcitonin and pan-culture if not already performed in last 24hrs

Features of COVID-19 Complications

CAC

Suspect if:

- INR >1.5
- Degree of PTT rise less than INR rise
- Platelets <100x109/L
- Fibrinogen ≤1.0g/L
- D-Dimer positive

ACTION:

✓ Ensure valid Group and Screen available



Cytokine Storm

Suspect if:

- Temperature ≥38.4°C
- Pancytopenia (WCC <4x10⁹/L, Hgb <90g/ L, Plts <100x10⁹/L)
- Ferritin >2000mcg/L
- Triglycerides ≥1.5mmol/L
- Fibrinogen ≤2.5g/L



ACTION:

✓ Perform HScore (MedCalc)

Secondary Bacterial Infection

Suspect if:

- Increasing WCC (>10x10⁹/L)
- Temperature ≥38.5°C
- Significant clinical change in patient hemodynamics



ACTION:

- ⇒ Send Procalcitonin
- ⇒ Pan-culture if not done in last 24hrs
- ✓ Start broad-spectrum antibiotics

Viral Myocarditis

Suspect if:

- Significant clinical change in patient hemodynamics
- New heart rhythm



ACTION:

- → Send Troponin and BNP (if raised consider causes e.g. ischemia, PE)
- Do NOT routinely perform ECG
- √ ICU Doctor to consider POCUS TTE

Other Management Considerations

Management of hypotension and/or low urine output:

Efforts should be made to limit fluid administration where possible due to evidence that patients with COVID-19 may develop worse lung injury with positive fluid balance

- ICU doctor to assess need for further investigations for determination of fluid status
- Minimise crystalloid bolus volumes to 250mL aliquots
- Early institution of vasopressors to reduce fluid requirements
- Consider secondary bacterial infection or viral myocarditis (see above)

Management of change in heart rhythm (in otherwise stable patient):

- Do NOT routinely call for 12-lead ECG
- Do NOT routinely retake blood for electrolytes
- ICU Doctor to assess need for further investigations based on bedside ECG monitoring

Tapering of initial antibiotic therapy:

 Review need for antibiotics started on admission with results of procalcitonin and rationalise or stop where possible

Notes on Lab Tests / Rationale and References for

D-Dimer Why are we tracking D-Dimer levels?	 Moderate evidence in multiple studies that elevation on admission >1000mcg/L is independent risk factor for mortality¹ - OR=18.42 (2.64-128.55; p=0.003) 168 Wuhan cases: median level in survivors 610mcg/L (highest level 1290), non-survivors median 2120mcg/L (770-5270)² 449 patients in Wuhan: D-Dimer, prothrombin time were positively, and platelet count was negatively, correlated with 28-day mortality in multivariate analysis (D-Dimer >3000mcg/L 52.4%, P=0.017). Better prognosis with heparin treatment.³
LFTs are abnormal in many patients, why not do them daily?	 Elevation in AST, ALT does not correlate with mortality⁴ Unclear whether a measure of viral load and direct viral liver inflammation or elevations due to drug toxicity, cytokine storm or hypoxemia: seen in 14-53% of patients (2-11% had liver comorbidities)⁵
Ferritin Why are we tracking Ferritin levels?	 Conflicting evidence: appears to be higher in more severe cases but not clear if useful predictor of mortality Median non-survivors 1435 (728-2000) vs 503 (<920)¹ Correlates with ARDS but not mortality: non-survivors median 1029 (546-2000) vs survivors median 457 (<700)⁶ COVID-19 may precipitate a cytokine storm/secondary HLH syndrome (no clear cases yet due to difficulty in diagnosis)⁻; a ferritin of >2000 (HScore) would raise suspicion of this diagnosis and help to highlight cases who may benefit from immunosuppression
Troponin Why do a troponin on admission and not trend it further?	 Prognostic but different assays and normal ranges limit external validity Non-survivors have significantly higher levels but still often within the normal range^{1,4}
Procalcitonin Why check a PCT on admission?	 Levels <0.5ng/mL in 95% of patients presenting with Covid-19 and does not correlate with severity of disease (using a primary outcome of death/ventilation/ICU admission)⁹ Consider an alternative diagnosis and prioritise standard sepsis treatment if level >0.5ng/mL Later in course of disease can be used to assess if chance of superadded bacterial infection

References:

- 1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 10.1016/S0140-6736(20)30566-3.
- 2. Tang N, Li D, Wang X, et al. Abnormal Coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. Journal of Thrombosis and Haemostasis. 10.1111/jth.14768
- 3. Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. Journal of Thrombosis and Haemostasis. https://doi.org/10.1111/jth.14817
- 4. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med (2020). https://doi.org/10.1007/s00134-020-05991-x
- 5. Zhang C, Shi L, Wang F, et al. Liver injury in COVID-19: management and challenges. Lancet Gastroenterology and Hepatology. https://doi.org/10.1016/ S2468-1253(20)30057-1
- 6. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. Published online March 13, 2020. doi:10.1001/jamainternmed.2020.0994
- Mehta P, McAuley D, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. The Lancet. https://doi.org/10.1016/S0140-6736(20)30628-0
- 8. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585
- 9. Guan W, Ni Z, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. NEJM. 10.1056/NEJMoa2002032