COVID-19: Highlights of Emerging Evidence for ICUs

As of 16 April 2020

The publications below have been selected from three sources: (i) a search of COVID-19 literature published since 08 April 2020, (ii) websites publishing COVID-19 rapid reviews (Cochrane, CEBM, Evidence Aid, HSE Ireland), (iii) 'hand' search of specific websites for grey literature resources.

This is not a full systematic review of all published literature and not a clinical guideline but an update of latest published studies

Focus: Haemostasis and Thrombosis - implications for practice emerging this week

- Apply pharmacological thrombosis prophylaxis in all COVID-19 patients admitted to ICU. Consider appropriate dosing and be vigilant for thrombosis occurrence. *(Source 2)*
- Re-assessing VTE and bleeding risks regularly is essential. *(Source 1)*
- Haematologists should consider enabling the use of the DIC (disseminated intravascular coagulation) score in the clinical assessment of patients hospitalised with COVID-19, as a marker of disease severity. *(Source 3)*

Publications:

1. Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19

Retrospective analysis of data from 1026 patients with lab-confirmed COVID-19 from a nationwide administrative dataset in China

- **Incidence: 40%** high risk for VTE. Among these patients, **11%** (of the 40%) also had high risk of bleeding, requiring adjustment to VTE prevention strategy.
- **Diagnostics:** VTE risk evaluated on admission via the Padua Prediction Score.
- **Management recommendations**: patients with COVID-19 can rapidly develop physiological changes which mean their need for prophylaxis changes. Assessing VTE and bleeding risks regularly is essential.

Published: 09/04/2020
Accessible: https://www.thelancet.com/pdfs/journals/lanhae/PIIS2352-3026(20)30109-5.pdf

2. Incidence of thrombotic complications in critically ill ICU patients with COVID-19

Retrospective analysis of data from 184 COVID-19 ICU patients from 3 Dutch hospitals

- **Incidence: 31%** of thrombotic complications in 184 COVID-19 patients admitted to 3 Dutch ICUs.
- **Diagnostics:** composite outcome of symptomatic acute pulmonary embolism, deep-vein thrombosis, ischemic stroke, myocardial infarction or systemic arterial embolism.
- **Management recommendations**: strictly apply pharmacological thrombosis prophylaxis in all COVID-19 patients admitted to ICU. Strongly suggestive to increase the prophylaxis towards high-prophylactic doses, even in the absence of randomised evidence.

Published: 10/04/2020
Accessible: https://www.sciencedirect.com/science/article/pii/S0049384820301201

3. Disseminated intravascular coagulation (DIC) score is of prognostic value in COVID-19 pneumonia

Guidelines on DIC score by British Society for Haematology evidenced by single-centre study of 183 COVID-19 patients from Wuhan, China

- **Incidence: 71%** of non-survivors had overt DIC, compared with only 0.6% of survivors.
- **Diagnostics**: ISTH diagnostic criteria for DIC score calculated from measurement of; platelet count, D-dimer, fibrinogen and prothrombin time.
- **Management recommendations**: The presence of DIC correlates with more severe disease and mortality. Haematologists should support use of the score in the clinical assessment of patients hospitalised with proven COVID-19 infection.

Published: 01/04/2020
Accessible: https://b-s-h.org.uk/media/18206/dic-score-in-covid-19-pneumonia_01-04-2020.pdf

4. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Single-centre retrospective study of 449 severe COVID-19 patients in Wuhan, China

- **Incidence:** 28-day mortality of heparin users were lower than non-users in patients with SIC score >4 (**40%** vs 64.2% p=0.029) or D-dimer >6x upper limit of normal (**32.8%** vs 52.4% p=0.017)
- **At risk:** severe COVID-19 patients (respiratory rate≥30 breaths /min; Arterial oxygen saturation ≤93% at rest; PaO2/FiO2≤300 mmHg)
- **Diagnostics:** SIC (sepsis induced coagulopathy) score system: includes PT, platelet count and sequential organ failure assessment (SOFA). Coagulation dysfunction defined as: sepsis induced coagulopathy (SIS) score >4 or D-dimer >6x upper limit of normal
- **Management recommendations**: In severe COVID-19 patients meeting SIC criteria or with markedly elevated D-dimer (n=97), anticoagulant therapy mainly with LMWH appears to be associated with better prognosis.
- No mortality benefit in patients with SIS score <4 or D-dimer <6x upper limit of normal.

Published: 27/03/2020
Accessible: https://onlinelibrary.wiley.com/doi/10.1111/jth.14817

Cardiac and arrhythmic complications in patients with COVID-19

Evidence review of 5 cohort studies evaluating cardiac manifestations in SARS-CoV-2 (COVID-19). Review also compared 4 cohort studies on SARS-CoV, 4 cohort studies on MERS-CoV and 1 cohort study on H1N1

- Increasing clinical and epidemiological evidence suggests that COVID-19 infection is associated with myocardial injury and arrhythmic complications.
- Prevalence of COVID-19 arrhythmogenic effects has yet not been reported, close cardiovascular surveillance is advisable, particularly in patients with more severe presentation and those with increased baseline risk due to previous cardiac comorbidities.
- Since many medications are being used empirically to treat the infection and/or symptoms, there is a need to increase awareness to possible drug interactions and close monitoring in atrioventricular conduction and QT interval.

Published: 09/04/2020
Accessible: https://onlinelibrary.wiley.com/doi/full/10.1111/jce.14479

GUIDANCE: Conscious pronation: Intensive Care Society (ICS)

- **Why**: In ventilated patients with moderate-severe ARDS prone position improved ventilation and mortality when compared to conventional supine ventilation (PROSEVA trial). Postulated that adopting prone position for conscious COVID-19 patients requiring basic respiratory support may also be beneficial for improving oxygenation, reducing need for invasive ventilation and potentially reducing mortality.
- **Advantages**: Regardless whether intubated or not: improved VQ matching and reduced hypoxaemia, reduced shunt, recruitment of posterior lung segments due to reversal of atelectasis and improved secretion clearance.
- **Consider if**: Can communicate with patient, patient can rotate independently, no anticipated airway issues.
- **Contraindications**: Respiratory distress, immediate need for intubation, haemodynamic instability, altered CNS or irritability, unstable spine/thoracic injury/recent abdominal injury, facial injury, neurological issues, morbid obesity, pregnancy, pressure sores.
- **Practical notes**: Monitor O2 saturations for 15 mins after every position change. Position change every 1-2hrs. Stop if patient desaturating, respiratory distress or non-tolerance.

Published: 12/04/2020
Accessible: https://www.ics.ac.uk/ICS/ICS/GuidelinesAndStandards/COVID19_Guidance.aspx

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Appendix: Published rapid reviews

Oxford Rapid Review: Hydroxychloroquine for COVID-19. What do the clinical trials tell us?

- Current data do not support the use of hydroxychloroquine for prophylaxis or treatment of COVID-19.

Published: 14/04/2020
Accessible: https://www.cebm.net/covid-19/hydroxychloroquine-for-covid-19-what-do-the-clinical-trials-tell-us/

Oxford Rapid Review: N-acetylcysteine (NAC): a rapid review of the evidence for effectiveness in treating COVID-19

- No COVID-specific evidence for NAC, so Oxford group has looked at evidence in other acute respiratory disorders that involve an oxidative stress.
- Clinical trial evidence for the use of NAC as an antioxidant in influenza and other acute viral respiratory tract infections is very limited and therefore difficult to draw any concrete conclusions without further trial evidence.

Published: 14/04/2020
Accessible: https://www.cebm.net/covid-19/n-acetylcysteine-a-rapid-review-of-the-evidence-for-effectiveness-in-treating-covid-19/

Oxford Rapid Review: Lopinavir/ritonavir: a rapid review of the evidence for effectiveness in treating COVID-19

- There is currently no strong evidence of efficacy of Lopinavir/ritonavir in the treatment of COVID-19. Several ongoing trials of Lopinavir/ritonavir are currently recruiting.

Published: 14/04/2020
Accessible: https://www.cebm.net/covid-19/lopinavir-ritonavir-a-rapid-review-of-the-evidence-for-effectiveness-in-treating-covid/

Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review

Evidence review of observational data and small clinical trials (<250 patients)

- No therapies have been shown effective to date.

Published: 13/04/2020
Accessible: https://jamanetwork.com/journals/jama/fullarticle/2764727