



Covid-19/Influenza-Associated Pulmonary Aspergillosis - Management

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Patients with acute respiratory distress syndrome (ARDS) and/or ICU treatment under mechanical ventilation due to suspected pneumonia^{1,2}

DIAGNOSIS BUNDLE

- ✓ Day (D)0+2 – Chest CT (if feasible)
- ✓ D0 – Bronchoalveolar lavage (BAL) → inspection of trachea and bronchi (consider risk of aerosolization of SARS-CoV-2) or tracheal aspirate (TA)
 - Virology: Respiratory viruses incl. SARS-CoV-2 & Influenza A/B
 - Microbiology: direct microscopy, culture, susceptibility, bacterial & fungal (*Aspergillus* spp.) specific PCR, galactomannan (GM) from BAL/TA fluid, if available: IMMY™ *Aspergillus* lateral flow assay (LFA)
- ✓ If SARS-CoV-2 or Influenza A/B positive → serum GM, IMMY™ *Aspergillus* LFA and β-D-glucan screening (if available)³ 3x/week until discharge from ICU or defervescence for ≥7 days with improved lung function
- D7±3 w/o improvement: BAL → inspection of trachea and bronchi (consider risk of aerosolization of SARS-CoV-2)
 - ✓ Microbiology: direct microscopy, high volume culture, susceptibility testing of min. 5 isolates or use screening agar with azoles plus specific fungal PCR (*Aspergillus* spp.); GM from BAL/TA fluid⁴

One of the following signs or symptoms triggers a repeat chest CT after 7 days⁵

- Infiltrates or specific invasive Aspergillosis (IA) signs on prior chest CT
- Microbiological findings indicative of IA
- Refractory fever ≥3 days of appropriate antibiotic therapy
- New fever after a period of defervescence of ≥48 hours while still on antibiotics without other cause
- Haemoptysis
- Pleural friction rub or chest pain
- Worsening respiratory insufficiency despite appropriate antibiotic therapy and ventilator support

TREATMENT BUNDLE

COVID-19^{6, 7}

- ✓ Remdesivir 200mg loading dose, followed by 100mg QD iv can be considered on a case-by-case basis. Alternatively use local standard of care

INFLUENZA A/B⁸

- ✓ Oseltamivir 75mg BID po – ≥5 days
- ✓ Oseltamivir 105mg or 150mg BID po can be considered during pregnancy
- ✓ Steroids for influenza treatment have been associated with increased mortality → not recommended unless indicated for known adrenal insufficiency

COVID-19/INFLUENZA-ASSOCIATED PULMONARY ASPERGILLOSIS (CAPA/IAPA)^{9, 10}

- ✓ 1st-line options: voriconazole (loading dose 6mg/kg BW BID, iv on D1; D2 4mg/kg BW BID, iv) or isavuconazole (loading dose 200mg TID, iv D1+2 (6 doses); D3 200mg QD, iv)
- ✓ Consider local resistance situation
- ✓ 2nd-line options in refractory cases or when 1st-line options contraindicated/not feasible: liposomal amphotericin B (3mg/kg BW QD, iv), posaconazole (300mg BID, iv on D1; D2 300mg QD, iv), echinocandins
- ✓ Refractory disease: switch or add antifungal class

THERAPEUTIC DRUG MONITORING (TDM) – weekly (2x in first week)⁹

- ✓ Voriconazole: Target plasma trough concentration: 1-5.5mg/L
- ✓ Posaconazole: Target plasma trough concentration: >1mg/L
- ✓ Isavuconazole: No target level available, but TDM may help explain failure

ARDS-MANAGEMENT¹¹⁻¹³

- ✓ Use lung protective ventilation
- ✓ Sufficient positive end-expiratory pressure (PEEP) on the ventilator may prevent alveolar collapse and facilitate the recruitment of unstable lung regions
 - ✓ CAVEAT: PEEP decreases venous return to the heart and can cause hemodynamic instability. Alveolar overdistention can be caused by excessive PEEP, that furthermore reduces respiratory-system compliance
- ✓ Consider prone positioning during mechanical ventilation in patients with severe ARDS (≥16 hours per day)^{14, 15}
- ✓ Consider vVECMO as rescue strategy in patients with refractory respiratory failure. However, it is currently unknown if it is beneficial during COVID-19 triggered cytokine storm or hypercoagulability