Aspergillus infection in patients supported with extracorporeal membrane oxygenation (ECMO)

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Aspergillus infection in critically-ill patients

• Incidence Invasive Aspergillosis (IA) ICU: 0.3-5.8%.
• High mortality, independent of invasive disease or colonization.
• Influenza infection is associated with IA (≈23% H1N1 patients)\(^1\).
• EORTC/MSG definition of IA not validated in critically ill patients.

  • Recognised in patients who lack host risk factors.
  • Non-invasive diagnostic methods not validated in immunocompetent patients.
  • Difficult to interpret radiological changes.
  • Difficult to perform invasive diagnostic procedures.

Aspergillus infection in critically-ill patients

**Proven IA:** Histopathology + culture

**Putative IA:**
- BAL positive for *Aspergillus* spp
- *Either*
  - Host risk factors
  - Positive cytological exam
- Signs and/or symptoms and abnormal chest radiology

**Aspergillus colonization:** No clinical or microbiological criteria for Putative IA.

Sensitivity 92%, Specificity 61%

Blot et al. *Am J Respir Crit Care Med*, 2012;186:56-64
Aspergillus infection in ECMO

- ELSO registry (1985—2009) included 46 patients\(^1\).
  - No differentiation between colonization or infection
  - Mortality at hospital discharge 70%.

- Aubron et al (2005-2011) included 11 patients\(^2\).
  - Higher incidence on ECMO than ICU.
  - Overall mortality rate was 74%.

Aspergillus infection in patients supported with ECMO

- Retrospective service evaluation patients supported with ECMO from October 2014 to May 2016 (20 months).

- **Aims:**
  - Determine the incidence and outcome of IA among ECMO patients.
  - Assess the value of GM and *Aspergillus* PCR in BAL for diagnosis of IA in ECMO patients.
  - Investigate the relationship between IA and *Influenza* infection.

- Data collected included epidemiological data, microbiological cultures, radiographic findings and outcomes.

- Cases were classified as proven IA, putative IA or *Aspergillus* colonization.
- 64 patients, 34 males (53%)
- Mean age 46.3 ± 26 years
- Mean of days on ECMO support: 15.1 ± 11 days.

**Diagnosis on admission**

- Pneumonia: 49%
- Influenza A infection: 18%
- ARDS (Non-infectious cause): 28%
- Asthma exacerbation: 5%

ARDS: Acute Respiratory Distress Syndrome
64 patients with ECMO support

11 Aspergillus isolation in lower respiratory tract samples

- 7 Putative Invasive Aspergillosis
- 4 Aspergillus colonization

53 patients did not have Aspergillus isolated

- 12 (23%) had Influenza infection
- None had Influenza co-infection

5 (71%) had Influenza co-infection

- Incidence of Putative Invasive Aspergillosis: 11%.
- Incidence of Aspergillus colonization: 6%. 
### 7 patients with Putative Invasive Aspergillosis

<table>
<thead>
<tr>
<th>Aspergillus species</th>
<th>Sample site</th>
<th>BAL cytological exam</th>
<th>Signs and/or symptoms and abnormal chest radiology</th>
<th>Host risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A. fumigatus</td>
<td>BAL</td>
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<td>7. A. fumigatus</td>
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</table>
**4 patients with *Aspergillus* colonization**

<table>
<thead>
<tr>
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<th>Aspergillus species</th>
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<th>BAL cytological exam</th>
<th>Signs and/or symptoms and abnormal chest radiology</th>
<th>Host risk factors</th>
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<tr>
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<td>A. fumigatus</td>
<td>BAL</td>
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</tbody>
</table>
• BAL Galactomannan
  • Putative IA:
    • Requested in 4/7
      • Positive in 4/4 (100%) (GM range 7-10.1).
  • Patient without evidence of *Aspergillus*:
    • Requested in 22/53 (42%).
      • Positive in 4/22 (18%) (GM range 0.7-1.8)
      • Negative in 18/22 (82%) (GM <0.5)

• BAL *Aspergillus* PCR
  • Putative IA:
    • Requested in 5/7
      • Positive in 4/5 (80%) (Ct value range 29.4-34.7)
Outcomes

- 64 patients with ECMO support:
  - Mortality on ECMO: 25% (n=16).
  - **Overall 3-month mortality: 39% (n=25)**

- 11 patients with evidence of *Aspergillus* in airways.
  - Putative invasive aspergillosis:
    - **3-month mortality: 5/7 (71%).**
  - *Aspergillus* colonization:
    - **3-month mortality: 1/4 (25%).**
Conclusions:

- Critically-ill patients supported with ECMO are at high risk of developing *Aspergillus* infection.

- IA is a potential complication of severe *Influenza* infection in this group of patients.

- *Aspergillus* infection is associated with high mortality among patients supported with ECMO.

- New validated diagnostic criteria for IA in critically-ill patients allow to identify affected patients who lack the classical risk factors of IA.
Future work

• Antifungal prophylaxis on patients who receive ECMO for Flu A.

• Validation of BAL GM in critically ill, non-immunosuppressed patients and incorporation in diagnostic criteria for IA

• Optimal antifungal dosing in ECMO.

• Immune defects resulting from Flu and ECMO.
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Thank you for your attention

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