

## Supplement 2. Definition of invasive pulmonary aspergillosis for different population

Author/ Abbreviation	Population	Definition
Donnelly et al <sup>1</sup> EORTC/MSG definition in 2020	The category of proven IFD can apply to any patient, and the probable and possible categories are proposed for immunocompromised patients	Proven
		Meeting one of the following: 1. Detection of aspergillus by microscopic analysis or culture of sterile material 2. Positive tissue nucleic acid test of <i>Aspergillus</i> species
		Probable
		Meeting all three criteria as following: 1. Host factors: meeting one of the following a: Neutropenia( $<0.5 \times 10^9$ for $>10$ days) b: Hematologic malignancy c: Receipt of an allogeneic stem cell transplant d: Receipt of a solid organ transplant e: Corticosteroids( $\geq 0.3$ mg/kg for $3 \geq$ weeks) f: T-cell immunosuppressants g: B-cell immunosuppressants h: Inherited severe immunodeficiency i: Acute graft-versus-host disease grade III or IV 2. Clinical features: At least one pattern on pulmonary CT (e.g., dense, air crescent sign, cavity) 3. Mycological evidence: meeting one of the following a: GM antigen positive on blood, BAL, or CSF b: Two or more PCR tests positive on blood or BAL c: Positive culture of <i>Aspergillus</i> species from sputum, BAL, aspirate, or bronchial brush

		Possible
		Meet the criteria of the probable but not for mycological evidence
Blot et al <sup>2</sup> <i>Asp</i> ICU classification	Patients in ICU	Proven
		Same as the proven definition of EORTC/MSG criteria
		Putative
		Meeting all four criteria as following: <ol style="list-style-type: none"> <li>1. Positive culture of <i>Aspergillus</i> species from LRT specimen</li> <li>2. Signs or symptoms (e.g., refractory or recrudescence fever, pleuritic chest pain, pleuritic rub, or dyspnea)</li> <li>3. Abnormal pulmonary imaging by CT or chest X-ray</li> <li>4. a or b <ol style="list-style-type: none"> <li>a. Host factors: neutropenia, hematological, oncological malignancy, glucocorticoid treatment (20 mg/d) or immunodeficiency</li> <li>b. Positive culture of <i>Aspergillus</i> species from BAL with positive cytological smear</li> </ol> </li> </ol>
		Colonization
		≥ 1 criteria in the putative definition is lacked
Bulpa et al <sup>3</sup>	Patients with chronic obstructive pulmonary disease	Proven
		Detection of <i>Aspergillus</i> species by microscopic analysis accompanied with one of the following: <ol style="list-style-type: none"> <li>1. Positive culture of <i>Aspergillus</i> species from LRT specimen</li> <li>2. Positive antibody/antigen of <i>A. fumigatus</i> in serum</li> <li>3. Confirmation of hyphae <i>Aspergillus</i> species</li> </ol>
		Probable
		Meeting one of the following: <ol style="list-style-type: none"> <li>1. Without the evidence of 1, 2 or 3 in the proven definition</li> </ol>

		<p>2. Treated with steroids and on stage III or IV of GOLD, with advanced dyspnea and abnormal chest imaging, accompanied with one of the following:</p> <p>a: positive culture or microscopic analysis from LRT</p> <p>b: Serum antibody test of <i>Aspergillus</i> species</p> <p>c: Positive two serum GM tests</p>
		Possible
		Without the evidence of a, b or c in probable definition
		Colonisation
		Positive culture of <i>Aspergillus</i> species without clinical features
Husain et al <sup>4</sup> ISHLT definition	Cardiothoracic transplant recipients	Proven
		Detection of aspergillus by microscopic analysis, or positive culture of <i>Aspergillus</i> species from sterile material of pulmonary site
		Probable
		Meeting all four criteria as following:
		<ol style="list-style-type: none"> <li>1. Sign/symptoms (e.g., Fever or hypothermia without recognized cause; leukopenia or leukocytosis; purulent sputum; pleural effusion; or worsening gas exchange)</li> <li>2. Radiology (e.g., New or progressive and persistent infiltrate, consolidation, cavitation, or nodules)</li> <li>3. Laboratory (e.g., positive culture/PCR from BAL/blood; positive GM test of BAL; or no less than two positive culture/PCR from sputum)</li> <li>4. Negative histology</li> </ol>
Koehler et al <sup>5</sup> ECMM/ISHAM consensus criteria	Patients with COVID-19	Proven
		Meeting three criteria as following
		<ol style="list-style-type: none"> <li>1. Host factors: diagnosed with COVID-19 needing intensive care</li> <li>2. Mycological evidence: detection of aspergillus by microscopic analysis, or</li> </ol>

		positive culture/PCR from sterile material of pulmonary site
		Probable
		Meeting three criteria as following 1. Host factors: diagnosed with COVID-19 needing intensive care 2. Clinical factors: pulmonary infiltrate or cavitating infiltrate on CT without other reason 3. Mycological evidence: meeting one of criteria as following a: Detection of aspergillus by microscopic analysis, or positive culture from BAL b: Serum GM/LFA index >0.5, or BAL GM/LFA index >1, or more than two positive PCR of blood, or single positive PCR of BAL with/without single positive PCR of blood
		Possible
		meeting three criteria as following 1. Host factors: diagnosed with COVID-19 needing intensive care 2. Clinical factors: pulmonary infiltrate or cavitating infiltrate on CT without other reason 3. Mycological evidence: meeting one of the following a: Positive microscopic analysis/positive culture from non-BAL material b: Single GM index of non-BAL material >4.5 c: More than one GM index of non-BAL material >1.2 d: Single GM index >1.2 plus positive LFA/PCR of non-BAL material
Schauwvlieghe et al <sup>6</sup> modified AspICU classification	Patients with influenza in ICU	Meeting three criteria as following: 1. Clinical criteria (e.g., refractory/recrudescent fever despite antibiotic therapy for at least three days without recognized reason, dyspnea, or haemoptysis) 2. Radiological criteria: infiltrate on pulmonary imaging

		<p>3. Mycological criteria: meeting one of the following</p> <p>a: Detection of hyphae by microscopic analysis with positive culture from tissue</p> <p>b: Positive culture from BAL</p> <p>c: BAL GM index&gt;1 or serum GM index&gt;0.5</p>
Verweij et al <sup>7</sup> IAPA definition	Patients with influenza in ICU	Proven
		Meeting two criteria as following: <ol style="list-style-type: none"> <li>1. Host factors: diagnosed with influenza</li> <li>2. Detection of <i>Aspergillus</i> species by microscopic analysis or positive culture/PCR from tissue</li> </ol>
		Probable <ol style="list-style-type: none"> <li>1. Pulmonary infiltrate companied with serum GM index&gt;0.5/BAL GM index&gt;1/positive BAL culture</li> <li>2. Cavitating infiltrate Cavitating infiltrate companied with positive sputum/tracheal aspirate culture</li> </ol>

**Abbreviations:** EORTC/MSG = European Organization for Research and Treatment of Cancer and the Mycoses

Study Group; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IFD = invasive fungal disease; GM = galactomannan; CT = computerized tomograph; BAL = bronchoalveolar lavage; CSF = cerebrospinal fluid; ICU = intensive care unit; LRT = lower respiratory tract; ISHLT = International Society for Heart and Lung Transplantation; ECMM/ISHAM = European Confederation for Medical Mycology and the International Society for Human and Animal Mycology institution; COVID-19 = coronavirus disease 2019; LFA = lateral-flow assay; IAPA = influenza-associated pulmonary aspergillosis.

<sup>1.</sup> Donnelly JP, Chen SC, Kauffman CA, et al. Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. *Clin Infect Dis* 2020;71(6):1367-76.

<sup>2.</sup> Ascioğlu S, Rex JH, de Pauw B, et al. Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and

hematopoietic stem cell transplants: an international consensus. *Clin Infect Dis* 2002;34(1):7-14.

3. Bulpa P, Dive A, Sibille Y. Invasive pulmonary aspergillosis in patients with chronic obstructive pulmonary disease. *Eur Respir J* 2007;30(4):782-800.
4. Husain S, Mooney ML, Danziger-Isakov L, et al. A 2010 working formulation for the standardization of definitions of infections in cardiothoracic transplant recipients. *J Heart Lung Transplant* 2011;30(4):361-74.
5. Koehler P, Bassetti M, Chakrabarti A, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. *Lancet Infect Dis* 2021;21(6):e149-e62.
6. Schauwvlieghe A, Rijnders BJA, Philips N, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. *Lancet Respir Med* 2018;6(10):782-92.
7. Verweij PE, Rijnders BJA, Brüggemann RJM, et al. Review of influenza-associated pulmonary aspergillosis in ICU patients and proposal for a case definition: an expert opinion. *Intensive Care Medicine* 2020;46(8):1524-35.