CORRESPONDENCE



COVID-19 associated pulmonary aspergillosis: regional variation in incidence and diagnostic challenges

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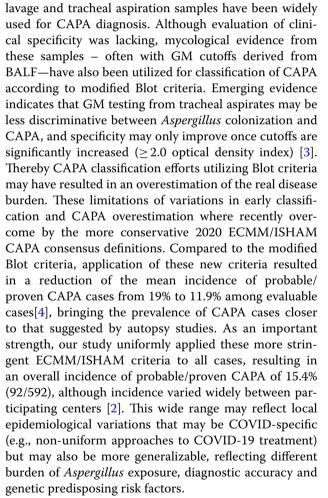
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We thank Rouze et al. for the thoughtful remarks [1] on our multinational study on pulmonary aspergillosis (CAPA) associated to coronavirus disease 2019 (COVID-19) [2].

We agree that diagnosis of CAPA is complex and requires incorporation of clinical presentation, imaging and mycological work-up with the additional challenge of possible diagnostic uncertainty in patients with acute respiratory failure. Further, diagnostic strategies vary widely between centers and systemic CAPA screening is rarely performed, as shown in our study where even serum galactomannan (GM) levels were available in less than half of patients (277/592) [2]. This scarce may be a result of low serum GM sensitivity (19%) [2] reflecting the primary airway invasive character of the disease with delayed angioinvasion, mirroring pathophysiology of aspergillosis in other non-neutropenic populations. Consequently, mycological evaluation of respiratory specimens is key for early diagnosis and successful management of CAPA. While bronchoalveolar lavage fluid (BALF) has been the benchmark specimen for diagnosing aspergillosis in the non-neutropenic host, BALF samples have not been widely available from COVID-19 patients due to safety concerns in the early phase of the pandemic (BALF was obtained in about half of our cohort [2]). Thus, other respiratory specimens such as non-bronchoscopic

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Detailed evaluation of our cohort has indicated older age, need for invasive respiratory support and receipt of tocilizumab as independent risk factors associated with



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development of CAPA, and presence of CAPA represented an independent factor for reduced probability of ICU survival, even after controlling for underlying conditions [5].

Importantly our data reflect a real-life scenario with no predefined CAPA screening or fungal diagnostics strategies and despite enrolling prospectively, not all centers had CAPA and non-CAPA patients reported for the entire study period.

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Declarations

Conflicts of interest

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References

- Rouze A, Lemaitre E, Nseir S (2021) COVID-19-associated pulmonary invasive aspergillosis: high incidence or difficult diagnosis? Intensive Care Med. https://doi.org/10.1007/s00134-021-06499-8
- Prattes J, Wauters J, Giacobbe DR, Lagrou K, Hoenigl M, Group E-CS (2021) Diagnosis and treatment of COVID-19 associated pulmonary apergillosis in critically ill patients: results from a European confederation of medical mycology registry. Intensive Care Med
- Roman-Montes CM, Martinez-Gamboa A, Diaz-Lomeli P, Cervantes-Sanchez A, Rangel-Cordero A, Sifuentes-Osornio J, Ponce-de-Leon A, Gonzalez-Lara MF (2021) Accuracy of galactomannan testing on tracheal aspirates in COVID-19-associated pulmonary aspergillosis. Mycoses 64:364–371
- 4. Fekkar A, Neofytos D, Nguyen MH, Clancy CJ, Kontoyiannis DP, Lamoth F (2021) COVID-19-associated pulmonary aspergillosis (CAPA): how big a problem is it? Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases
- 5. Prattes J, Wauters J, Giacobbe DR, Salmanton-Garcia J, Maertens J, Bourgeois M, Reynders M, Rutsaert L, van RegenmortelN, Lormans P, Feys S, Reisinger AC, Cornely OA, Lahmer T, Valerio M, Delhaes L, Jabeen K, Steinmann J, Chamula M, Bassetti M, Hatzl S, Richardson R, Lagrou K, Hoenigl M (2021) Risk factors and outcome of pulmonary aspergillosis in critically ill coronavirus disease 2019 patients– a multinational observational study by the European Confederation of Medical Mycology.Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and InfectiousDiseases. https://doi.org/10.1016/j.cmi.2021.08.014