Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
UPDATE IN RADIOLOGY

Spectrum of opportunistic fungal lung co-infections in COVID-19: What the radiologist needs to know

A.V. Nair a,b,*, S. Ramanathan a,c, P. Sanghavi d, V. Manchikanti e, S. Satheesh f, M. Al-Heidous a, A. Jajodia g, D. Blair Macdonald g,h

a Departamento de Imagenología Clínica, Hospital Al-Wakra, Hamad Medical Corporation, Doha, Qatar
b Departamento de Radiología Clínica, NHS Salisbury Foundation Trust, Salisbury, Wiltshire, United Kingdom
c Departamento de Radiología, Weill Cornell Medicine, Doha, Qatar
d Jankharia Imaging Centre, Mumbai, India
e Departamento de Radiología, Facultad de Medicina de Narayana, Nellore, India
d Departamento de Patología, Regional Cancer Center, Trivandrum, India
e Departamento de Radiología, Juravinski Cancer Center y St. Josephs Healthcare, Hamilton, Universidad McMaster, Ontario, Canada
h Departamento de Radiología, Universidad de Ottawa, Ontario, Canada

Received 29 January 2022; accepted 9 June 2022
Available online 27 October 2022

Abstract Fungal lung co-infections associated with COVID-19 may occur in severely ill patients or those with underlying co-morbidities, and immunosuppression. The most common invasive fungal infections are caused by aspergillosis, mucormycosis, pneumocystis, cryptococcus, and candida. Radiologists integrate the clinical disease features with the CT pattern-based approach and play a crucial role in identifying these co-infections in COVID-19 to assist clinicians to make a confident diagnosis, initiate treatment and prevent complications.

© 2022 SERAM. Published by Elsevier España, S.L.U. All rights reserved.

Keywords Aspergillosis; COVID-19; Candida; Cryptococcus; Mucormycosis; Pneumocystis; SARS-CoV-2

Palabras clave Aspergilosis; COVID-19; Cándida; Criptococo; Mucormicosis;

Espectro de coinfecciones pulmonares fúngicas oportunistas en COVID-19: lo que el radiólogo debe saber

Resumen Las coinfecciones pulmonares fúngicas asociadas a la COVID-19 pueden ocurrir en pacientes gravemente enfermos o con comorbididades subyacentes e inmunosupresión. Las infecciones fúngicas invasivas más comunes son causadas por aspergilosis, mucormicosis, y las...
Key points

- Fungal co-infections in COVID-19 are the saprophytic type, commonly associated with immunocompromised status.
- Prolonged immunosuppression treatment and underlying co-morbidities predispose patients with COVID-19 to fungal lung infection.
- Clinical disease presentation, and CT pattern recognition can help identify and differentiate opportunistic fungal lung infections on a background of underlying COVID-19 pneumonia.

Introduction

The COVID-19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has had significant clinical, social, and economic implications around the globe. The viral infection is accompanied by an aggressive immunological response and cytokine storm that results in an excessive inflammatory reaction. Immunosuppressive treatment including the use of steroids have been advocated in severely and critically ill patients to prevent morbidity and mortality associated with COVID-19. In some cases, indiscriminate use of immunosuppressive drugs or steroids in COVID-19 has led to complications including opportunistic infections. COVID-19 treatment-related immunosuppression, underlying comorbidity related to malignancies, diabetes mellitus, human immunodeficiency virus, indwelling prosthesis, burns, and neutropenia, etc., has led to fungal co-infections with increased morbidity and mortality. Fungal co-infections are difficult to diagnose on a background of severe parenchymal lung disease from COVID-19 pneumonia. Radiological signs associated with fungal infections such as the halo sign and reverse halo sign are also seen with COVID-19 pneumonia.

Radiologists may be the first to raise the suspicion of fungal infections when reviewing CT scans of patients under acute treatment for COVID-19 or in post-COVID-19 follow-up. In this pictorial essay, we systematically present the most common features and differential diagnosis related to fungal co-infections on Chest CT of COVID-19 patients.

Fungal infections and the host immunity

There is a wide spectrum of bacterial and fungal infections that can develop in a patient with COVID-19 infection, due to underlying co-morbidities, nosocomial infections, or ventilator-associated pneumonia. COVID-19 related fungal lung co-infections has been attributed to pathophysiological processes of: (a) Danger-associated molecular patterns (DAMP) triggered by SARS-CoV-2 infection through impaired immunological response culminating in acute pulmonary injury; (b) Anti-viral immunity activation which creates a permissive environment for the proliferation of fungal organisms and; (c) Severe acute respiratory distress syndrome with a bed of interstitial and alveolar edema that serves as an environment for opportunistic lung infection to develop.

Classification of pulmonary fungal infections

Fungal infection involving the lungs can be broadly classified into 2 types, either saprophytic, which predominantly infects immunocompromised individuals (Pneumocystis jirovecii, candidiasis, aspergillosis, mucormycosis, cryptococcus), or pathogenic which predominantly infects immunocompetent individuals (coccidiomycosis,blastomycosis, histoplasmosis).

Fungal lung infections in COVID-19

The fungal lung infections that occur in COVID-19 are the saprophytic type infecting immunocompromised individuals. These patients tend to be symptomatic, while the clinical picture is often confusing and difficult to determine the presence of a fungal infection on a background of COVID-19. The reported incidence of co-infections associated with COVID-19 varies from 4% to 35%, for patients admitted in intensive care unit with acute respiratory distress syndrome. Most common pathogens are invasive pulmonary aspergillosis, mucormycosis, P. jirovecii, cryptococcus and candida infections. The spectrum of infection caused due to these opportunistic organisms ranges from indolent to aggressive and also depends on the underlying co-morbidities (Table 1).

The saprophytic fungal infections have a wide spectrum of disease patterns on the Chest CT including ground-glass opacities, consolidation, nodules, cysts, and cavitations (Fig. 1). Ancillary features of tracheobronchial wall thickening, mediastinal lymphadenopathy and pleural effusion may be present. A high index of suspicion and knowledge of the characteristic and overlapping patterns can help determine the presence of fungal co-infections. Often it is the reporting radiologist who raises the possibility of opportunistic fungal co-infection based on the Chest CT findings. Early detection
### Table 1  Predisposing factors associated with fungal lung infections.

| Organism                     | Predisposing associated conditions                                                                 |
|------------------------------|----------------------------------------------------------------------------------------------------|
| **CAPA**                     |                                                                                                    |
| Airway-invasive aspergillosis | Diabetes mellitus                                                                                    |
| Anglo-invasive aspergillosis  | Diabetes mellitus, neutropenia, HSCT allografts or solid organ transplants, hematological malignancies, prolonged steroids. |
| **CAM**                      |                                                                                                    |
|                               | Diabetes mellitus, hematological malignancies, solid organ transplants, chronic respiratory diseases, burns or local trauma. |
| *Pneumocystis jiroveci*       | HIV, patients with lymphopenia, solid organ transplants, hematological malignancies.                  |
| *Cryptococcus neoformans*    | Bird feces                                                                                          |
| Candida (White fungus)       | Hospitalization, indwelling venous catheter, hematological malignancy, peritoneal dialysis, post thoracic surgery |
| **CAM-SARS-COV-2**           | associated mucormycosis, **CAPA-SARS-COV-2** associated pulmonary aspergillosis, HIV — human immunodeficiency virus, HSCT— hematopoietic stem cell transplant |

Figure 1  COVID-19 pneumonia with typical imaging features. Axial chest CT images (lung window) in a 49 year old man (a, b) with real-time PCR positive result for SARS-COV-2 showing bilateral areas of multifocal consolidations (arrow) in a peripheral distribution. and clinical integration may allow for initiation of targeted treatment and improved care.

**Chest CT findings in COVID-19**

The most common reported findings of COVID-19 lung infection include ground glass opacities (GGO), consolidation, crazy-paving pattern, bilateral lung abnormalities, lower lobe and posterior predilection, and vascular engorgement\(^\text{25-27}\) (Fig. 2). The pattern of abnormality changes over time depending on the stage of the disease process.\(^\text{27}\) In early stage GGO is the predominant manifestation, crazy pavement in the progressive stage, consolidation in the peak stage, the consolidation may be completely absorbed or replaced by fibrotic changes in recovery stage.\(^\text{27}\) In a suspicious clinical scenario, with a positive test, or in a COVID-19 endemic region the presence of these findings should raise the suspicion for COVID-19.

**Chest CT findings in fungal co-infections with COVID-19**

**Aspergillus fumigatus**

*Aspergillus fumigatus* infects immunocompetent and immunocompromised individuals. SARS-COV-2-associated pulmonary aspergillosis (CAPA) has been one of the pre-dominant fungal infections in COVID-19 patients with acute respiratory distress syndrome (ARDS).\(^\text{28,29}\) CAPA manifests as either airway invasive aspergillosis, or angio-invasive aspergillosis (ANIA). The reported incidence of CAPA may vary depending on the treatment undertaken for severe or critically ill COVID-19 patients, especially with corticosteroids and anti-interleukin 6 (IL-6) like tocilizumab.\(^\text{30,31}\) CAPA is difficult to diagnose when the radiological findings related to aspergillosis resemble severe pulmonary manifestations of COVID-19.\(^\text{32,33}\) CAPA in critically ill or intubated patients is reported to have a mortality rate reaching up to 40%.\(^\text{34-38}\)

(a) **Angio-invasive aspergillosis (ANIA),** occurs exclusively in immunocompromised patients (Fig. 3). The organism invades small to medium-sized arteries and leads to solitary or multiple necrotic and hemorrhagic nodules, or infarcts. Chest CT demonstrates solitary or multiple pulmonary nodules and masses. The halo of hemorrhage may be seen as an area of ground-glass opacity surrounding the nodule referred as the halo sign. A reverse halo sign (defined as central ground-glass opacity surrounded by a crescentic or circumferential denser consolidation) may also be encountered. CT angiography may demonstrate vascular invasion.\(^\text{39}\) Lymph node enlargement or pleural effusion is usually absent. Confident diagnosis may be difficult because the halo sign and the reverse halo sign are also seen commonly with COVID-19 pneumonia. The presence of an obvious vascular invasion would prompt the radiologist to suspect ANIA co-infection on a background of COVID-19.

(b) **Airway invasive aspergillosis (AIA),** manifestations depend on the site of involvement within the airway. It may present as tracheobronchitis, bronchiolitis, or bronchopneumonia. Chest CT findings in tracheobronchitis include tracheal and bronchial wall thickening, bronchiolitis findings include centrilobular nodules with ‘tree-in-bud pattern’, while bronchopneumonia type of involvement seen as lobar or perihilar consolidation.\(^\text{40}\) When there is AIA co-infection in COVID-19, the tracheobronchitis and bronchiolitis type of involvement can be distinctly identified from the pattern of COVID-19 pneumonia, while the bronchopneumonia type might
be masked in severe or critical COVID-19 making the diagnosis difficult.

c. CAPA is difficult to diagnose on routine imaging in critical patients with COVID-19, as the imaging features are non-specific and, the typical features like halo sign or cavitation are rarely observed. Blood tests may be negative in AIA, in the non-neutropenic patient. Bronchoalveolar lavage (BAL) is rarely performed due to risk of transmission. Standard screening for fungal infections with serum galactomannan (GM) has low sensitivity of only 21% for detection of CAPA.

**Mucormycosis**

Mucormycosis is also known as 'black fungus' in the lay literature and is caused by inhalation of fungal spores that are present in the air, soil, compost, piles, decaying organic matter, fruits, or vegetables. Paranasal sinuses and lungs are the most affected sites. Diabetes mellitus is the most common risk factor, followed by immunosuppression, hematological malignancy, stem cell and organ transplantation. Chest CT findings are non-specific including the presence of nodules, consolidation, or ground-glass opacities (GGO). The reverse halo sign, lymphadenopathy, and/or pleural effusion may also be seen. The areas of consolidation may show cavitation on follow-up imaging. Rarely, mucormycosis may be associated with invasion of the pulmonary artery, superior vena cava, or other neck vessels (Figs. 4 and 5). The bird's nest sign refers to the appearance created by a reverse halo sign with associated irregular and intersecting areas of stranding or irregular lines within the area of ground-glass opacity. When the bird’s nest sign is
observed in the context of COVID-19 infection it should raise the suspicion for COVID-19 associated mucormycosis (CAM) infection. In practice, differentiating CAM from CAPA is difficult due to overlapping imaging features. The presence of bird’s nest sign, more than 10 lung nodules, pleural effusion, and concurrent sinus infections favors mucormycosis over invasive pulmonary aspergillosis. Bird’s nest sign is not specific for CAM and has been associated with cryptogenic organizing pneumonia, bacterial pneumonia, sarcoidosis, Wegener’s granulomatosis, paracoccidioidomycosis, pulmonary infarction.

Pneumocystis jirovecii

P. jirovecii is associated with acquired immunodeficiency syndrome, organ transplant recipients, and patients undergoing immunosuppressive treatment with chemotherapy or steroids. The risk of Pneumocystis jirovecii pneumonia (PJP) increases significantly with CD4+ lymphocytopenia (<200 cells/μL). SARS-COV-2 infection in an already immunosuppressed patient, leads to further functional immunosuppression predisposing the patient to PJP. Due to overlapping radiological features of SARS-COV-2 with PJP, the presence of PJP co-infection with SARS-COV-2 may be difficult to diagnose on imaging. The radiologists should approach the CT scan with suspicion for PJP co-infection in an immunocompromised patient with CD4+ lymphocytopenia. Typical CT findings include patchy or geographic GGO with predominant perihilar or middle zone predilection. Less frequently smooth interlobar septal thickening in a crazy-paving pattern may be present. Upper zone predominance can be seen in patients on prophylactic therapy. Peripheral sparing is described in 40% of patients giving a batwing appearance (Fig. 6). Pleural effusions are uncommon with this infection, and the presence of effusion should prompt the suspicion of other pathology or infection. During the chronic phase, the areas of lungs affected by crazy paving patterns may be replaced with irregular lung cysts, increasing the risk of pneumothorax in such cases. Less common findings encountered include pulmonary consolidation and centrilobular nodules. In patients with CD4+ lymphocytopenia, and imaging features that are suspicious for co-infection with PJP, it is recommended to suggest testing with serum beta-D-glucan, or quantitative polymerase chain reaction (PCR) for PJP.

Cryptococcus (Cryptococcus neoformans and C. gattii species)

These are commonly found in soil or bird droppings. SARS-COV-2 infection in patients with HIV accompanied by CD4+ lymphocytopenia (<200 cells/μL), or patients with stem cell transplants are susceptible to invasive cryptococcosis. Chest CT shows multiple pulmonary nodules of varying size (0.5 cm–4 cm), miliary pattern, or areas of consolidation (Fig. 7). Cavitation may occur within the nodules in immunocompromised patients. Pleural effusion or lymphadenopathy may also be seen. The clinical presentation with meningoencephalitis and Chest CT findings may be the first indication of invasive cryptococcosis co-infection.

Candida albicans

Candida also known as the ‘white fungus ’is an organism that is part of normal human microbial flora in the oral cavity. Most patients with pulmonary candidiasis tend to have widespread systemic involvement. Invasive candidiasis was shown to occur more frequently in patients who received broad-spectrum antibiotics, parenteral nutrition, prolonged neutropenia and other immune impairment factor. Pulmonary involvement with candida pneumonia is non-specific and on imaging is commonly attributed to other opportunistic infections or COVID-19 pneumonia. Chest CT
findings may include multiple solid nodules without a ground glass halo, GGO, miliary nodules, multifocal consolidation, or small pulmonary abscesses.66

Vigilance for opportunistic fungal infections in COVID-19

The typical imaging patterns associated with fungal infections overlap with COVID-19 pneumonia and other viral, bacterial infections and even malignancy. In some patients, radiologic manifestations may be delayed or absent. The radiologist has a role in integrating the high-risk clinical features, flagging the chest CT findings such as the halo sign, bird’s nest sign, cavitations, bronchial or peri-bronchovascular involvement associated with fungal co-infections and recommending confirmatory laboratory, or histopathological sampling.67 Sputum analysis, syndromic molecular panels with quantitative polymerase chain reaction, culture for aspergillosis, mucormycosis or P. jirovecii of respiratory samples may be performed to help confirm the diagnosis. Depending on the positivity further confirmatory testing with blood biomarkers, using serum galactomannan, serum beta-D-glucan, cryptococcal antigen, blood quantitative PCR for mucormycosis, and aspergillosis would be necessary.52,68 Biomarkers for diagnosing invasive aspergillosis, like galactomannan and beta-D-glucan are negative in patients with mucormycosis, allowing the clinical team to refine the diagnosis with the presence of contributing history and/or radiological suspicion.

Conclusion

COVID-19 patients with immunocompromised status and underlying comorbidities are prone to develop fungal co-infections. In a background of COVID-19, the radiologists should approach the chest CT with a high index of suspicion, for CAPA when there is history of steroid and interleukin-6 therapy, for CAM in diabetes mellitus, for PJP in HIV patients with CD4+ lymphocytopenia, and for cryptococcosis when there is pre-existing malignancies or immunosuppression associated with clinical presentation of meningoencephalitis. Most fungal lung co-infections in a setting of COVID-19 are invasive with a propensity for rapid deterioration. It is important for radiologists to be familiar with the typical and atypical disease pattern of fungal co-infection on chest CT in COVID-19 pneumonia patients, so that further workup including serology and tissue sampling can be performed to confirm the diagnosis and advance patient care.

Figure 7 Pulmonary cryptococcosis in a 54-year-old man receiving immunosuppressive treatment for past medical history of inflammatory bowel disease. Patient presents to emergency department with moderate COVID-19 symptoms. Chest CT on day-10, (a) axial CT image at the level of carina shows confluent nodules forming a mass like peri-bronchial consolidation with surrounding ground-glass opacities (arrows), (b) axial CT image showing multiple nodules with surrounding ground-glass halo in bilateral lower lobes (arrows), (c) axial CT image taken 2 weeks later shows complete lobar consolidation in the right lower lobe suggesting significant interval progression (arrow), (d) axial CT image of the thorax 2 months after the symptom onset and shows significant interval improvement with residual peri-bronchial consolidation in right lower lobe (arrow).
Authorship
1. Responsible for study integrity: MM, EP
2. Study conception: MM, EP, JCM, OJT, JCP
3. Study design: MM, EP
4. Data acquisition: MM, EP, JCM, OJT, JCP
5. Data analysis and interpretation: N/A
6. Statistical processing: N/A
7. Literature search: MM, EP, JCM, OJT, JCP
8. Drafting of the manuscript: MM, EP, JCM, OJT
9. Critical review of the manuscript with intellectually significant contributions: MM, EP, JCM, OJT, JCP
10. Approval of the final version: MM, EP, JCM, OJT, JCP

Funding
Authors has not received any funding for this article.

Conflicts of Interest
Authors have no disclosure or no relevant relationships.

References
1. Corticosteroids for COVID-19 [Accessed 10 April 2022]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1
2. Nair AV, Kumar D, Yadav SK, Nepal P, Jacob B, Al-Heidous M. Utility of coronary artery calcification on non-cardiac gated thoracic CT in predicting clinical severity and outcome in COVID-19. Clin Imaging. 2021;74:123-30, http://dx.doi.org/10.1016/j clinim.2021.01.015.
3. Tang Y, Liu J, Zhang D, Xu Z, Ji J, Wen C. Cytokine storm in COVID-19: the current evidence and treatment strategies. Front Immunol. 2020;11:1708, http://dx.doi.org/10.3389/fimmu.2020.01708.
4. Gangneux JP, Bougnoux ME, Dannaoui E, Cornet M, Zahar JR. Invasive fungal diseases during COVID-19: we should be prepared. J Mycol Med. 2020;30:100971, http://dx.doi.org/10.1016/j.jmym.2020.100971.
5. Duzgun SA, Durhan G, Demirkazik FB, Akpinar MG, Ariyurek OM. COVID-19 pneumonia: the great radiological mimicker. Insights Imaging. 2021;11:118, http://dx.doi.org/10.1007/s13244-020-00933-z.
6. Marchiori E, Zanetti G, Escuisatto DL, Souza AS, Meirelles GDSP, Fagundes J, et al. Reversed halo sign: high-resolution CT scan findings in 79 patients. Chest. 2012;141:1260-6, http://dx.doi.org/10.1378/chest.11-1050.
7. Primack SL, Hartman TE, Lee KS, Müller NL. Pulmonary nodules and the CT halo sign. Radiology. 1994;190:513-5, http://dx.doi.org/10.1148/radiol.190.2.8284408.
8. Alves GRT, Marchiori E, Iriton K, Nin CS, Watte G, Pasqualotto AC, et al. The halo sign: HRCT findings in 85 patients. J Bras Pneumol. 2016;42:435-9, http://dx.doi.org/10.1590/S1806-37562015000000029.
9. Arastehfar A, Carvalho A, van de Veerendonk FL, Jenks JD, Koehler P, Krause R, et al. COVID-19 associated pulmonary aspergillosis (CAPA) — from immunology to treatment. J Fungi. 2020;6:91, http://dx.doi.org/10.3390/jof6020091.
10. Tolle LB, Standiford TJ. Danger-associated molecular patterns (DAMPs) in acute lung injury. J Pathol. 2013;229:145-56, http://dx.doi.org/10.1002/path.4124.
11. Cunha C, Carvalho A, Esposito A, Bistoni F, Romani L. DAMP signaling in fungal infections and diseases. Front Immunol. 2012;3:286, http://dx.doi.org/10.3389/fimmu.2012.00286.
12. Padley SP, Rubens MB. Textbook of radiology and imaging. Churchill Livingstone; 2002. p. 153-60.
13. Yang X, Yu Y, Xu J, Shu H, Xia J, Lui H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Resp Med. 2020;8:475-81, http://dx.doi.org/10.1016/S2221-2600(20)30079-5.
14. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507-13, http://dx.doi.org/10.1016/S0140-6736(20)30211-7.
15. Schauwvliege AFAD, Rijnders BJA, Philips N, Verwijls R, Vanderbeke L, van Tienen C, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. Lancet Respir Med. 2018;6:782-92, http://dx.doi.org/10.1016/S2213-2600(18)30274-1.
16. Lamotch F, Glampedakis E, Bollat-Blanco N, Oddo M, Pagani JL. Incidence of invasive pulmonary aspergillosis among critically ill COVID-19 patients. Clinic Microbiol Infect. 2020;26:1706-8, http://dx.doi.org/10.1016/j.cmi.2020.07.010.
17. Rutsaert L, Steinfort N, van Hunsel T, Bomans P, Nae-sens R, Mertes H, et al. COVID-19-associated invasive pulmonary aspergillosis. Ann Intensive Care. 2020;10:71, http://dx.doi.org/10.1186/s13613-020-00686-4.
18. Kuehn BM. Pulmonary fungal infections affect patients with COVID-19. JAMA. 2020;324:2248, http://dx.doi.org/10.1001/jama.2020.22914.
19. Fekkar A, Lampros A, Mayaux J, Poignon C, Demeret S, Constantijn J, et al. Occurrence of invasive pulmonary fungal infections in patients with severe COVID-19 admitted to the ICU. Am J Resp Crit Care Med. 2021;203:307-17, http://dx.doi.org/10.1164/rccm.202009-3400oc.
20. Hoenigl M. Invasive fungal disease complicating coronavirus disease 2019: when it rains, it spores. Clin Infect Dis. 2021;73:e1645-8, http://dx.doi.org/10.1093/cid/ciaa1342.
21. Pasquier G, Bouniol A, Robert Gangneux F, Zahar JR, Gangneux JP, Novara A, et al. A review of significance of Aspergillus detection in airways of ICU COVID-19 patients. Mycoses. 2021;64:980-8, http://dx.doi.org/10.1111/myc.13441.
22. Lewis RE, Kontoyiannis DP. Invasive aspergillosis in glucocorticoid-treated patients. Med Mycol. 2009;47 Suppl 1:S271–81, http://dx.doi.org/10.1080/13693780802227159.
23. Bartoletti M, Pascale R, Cirrica M, Rinaldi M, Maccaro A, Bussini L, et al. Epidemiology of invasive pulmonary aspergillosis among intubated patients with COVID-19: a prospective study. Clin Infect Dis. 2021;73:e3606–14, http://dx.doi.org/10.1093/cid/ciaa1065.
24. Koehler P, Cornely OA, Böttiger BW, Dusse F, Eichenauer DA, Fuchs F, et al. COVID-19 associated pulmonary aspergillosis. Mycoses. 2020;63:528-34, http://dx.doi.org/10.1111/myc.13096.
25. Nair AV, McNnes M, Jacob B, Kumar D, Soman DK, Subair HSV, et al. Diagnostic accuracy and inter-observer agreement with the CO-RADS lexicon for CT chest reporting in COVID-19. Emerg Radiol. 2021;28:1045–54, http://dx.doi.org/10.1007/s10140-021-01967-6.

26. Nair AV, Ramanathan S, Venugopal P. Chest imaging in pregnant women with COVID-19: recommendations, justification, and optimization. Acta Radiol Open. 2022;11, http://dx.doi.org/10.1177/20584601221077394, 20584601221077394.

27. Kwée TC, Kwée RM. Chest CT in covid-19: what the radiologist needs to know. Radiographics. 2020;40:1848–65, http://dx.doi.org/10.1148/rg.2020200159.

28. Verweij PE, Gangeux JP, Bassetti M, Brüggemann RJM, Cornely OA, Koehler P, et al. Diagnosing COVID-19-associated pulmonary aspergillosis. Lancet Microbe. 2020;1:e53–5, http://dx.doi.org/10.1016/S2666-5247(20)30027-6.

29. Alanoio A, Dellèire S, Fodil S, Bretagne S, Mérabgarne B. Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. Lancet Respir Med. 2020;8:e48–9, http://dx.doi.org/10.1016/S2213-2600(20)30237-X.

30. Van Arkel AE, Rijpstra TA, Beelderbos HNA, van Wijngaarden P, Verweij PE, Bentvelsen RG. COVID-19-associated pulmonary aspergillosis. Am J Respir Crit Care Med. 2020;202:132–5, http://dx.doi.org/10.1164/rccm.202004-0381LE.

31. Henzler C, Henzler T, Buchheidt D, Nance JW, Weis CA, Vogelmann R, et al. Diagnostic performance of contrast enhanced pulmonary computed tomography angiography for the detection of angioinvasive pulmonary aspergillosis in immunocompromised patients. Sci Rep. 2017;7:4483, http://dx.doi.org/10.1038/s41598-017-04470-6.

32. Franquet T, Müller NL, Oikonomou A, Flint JD. Aspergillus infection of the airways: computed tomography and pathologic findings. Comput Assist Tomogr. 2004;28:10–6, http://dx.doi.org/10.1097/00004472-200401000-00002.

33. Blot S, Taccone FS, van den Abeele AM, Bulpa P, Meersseman W, Brusselaers N, et al. A clinical algorithm to diagnose invasive pulmonary aspergillosis in critically ill patients. Am J Respir Crit Care Med. 2012;186:56–64, http://dx.doi.org/10.1164/rccm.201111-1978oc.

34. Jenks JD, Mehta SR, Taplitz R, Aslam S, Reed SL, Hoenigl M. Point-of-care diagnosis of invasive aspergillosis in non-neutropenic patients: aspergillus galactomannan lateral flow assay versus aspergillus-specific lateral flow device test in bronchoalveolar lavage. Mycoses. 2019;62:230–6, http://dx.doi.org/10.1111/ymy.12881.

35. Van Grootveld R, van Paassen J, de Boer MGJ, Claas EJC, Kuipper EJ, van der Beek MT, et al. Systematic screening for COVID-19 associated invasive aspergillosis in ICU patients by culture and PCR on tracheal aspirate. Mycoses. 2021;64:641–50, http://dx.doi.org/10.1111/myc.13259.

36. Mejia Buritica L, Karduss Urueta AJ. Pulmonary mucormycosis. N Engl J Med. 2021;384:e69, http://dx.doi.org/10.1056/nejmrcm2030205.

37. Orlowski HLP, McWilliams S, Meltinick VM, Bhalla S, Lubner MG, Pickhardt PJ, et al. Imaging spectrum of invasive fungal and fungal-like infections. Radiographics. 2017;37:1119–34, http://dx.doi.org/10.1148/rg.2017160110.

38. Nam Da B, Kim TJ, Lee KS, Kim TS, Han J, et al. Pulmonary mucormycosis: serial morphologic changes on computed tomography correlate with clinical and pathologic findings. Eur Radiol. 2018;28:788–95, http://dx.doi.org/10.1007/s00330-017-5007-5.

39. Georgiadou SP, Sipsas NV, Marou EM, Kontoyiannis DP. The diagnostic value of halo and reversed halo signs for invasive mold infections in compromised hosts. Clin Infect Dis. 2011;52:1144–55, http://dx.doi.org/10.1093/cid/cir322.

40. Lee FYW, Mossad SB, Adal KA. Pulmonary mucormycosis: the last 30 years. Arch Intern Med. 1999;159:1301–9, http://dx.doi.org/10.1001/archinte.159.12.1301.

41. Vogl TJ, Hinrichs T, Jacobi V, Böhmke A, Hoelzer D. Computed tomographic appearance of pulmonary mucormycosis. RoFo. 2000;172:604–8, http://dx.doi.org/10.1055/s-2000-4647.

42. Walker CM, Abbott GF, Greene RE, Shepard J-AO, Vunmid D, Dingymathy SR. Imaging pulmonary infection: classic signs and patterns. AJR Am J Roentgenol. 2014;202:479–92, http://dx.doi.org/10.2214/ajr.13.11463.

43. Menon AA, Berg DD, Brea AJ, Deutsch AJ, Kidia KK, Thuber EG, et al. A case of COVID-19 and Pneumocystis jirovecii coinfection. Am J Respir Crit Care Med. 2020;202:136–8, http://dx.doi.org/10.1164/rccm.202003-0766LE.

44. Thomas CF Jr, Limper AH. Pneumocystis pneumonia. N Eng J Med. 2004;350:2487–98, http://dx.doi.org/10.1056/nejmra032588.

45. Kanne JP, Yandow DR, Meyer CA. Pneumocystis jirovecii pneumonia: high-resolution CT findings in patients with and without HIV infection. AJR Am J Roentgenol. 2012;198:W555–61, http://dx.doi.org/10.2214/ajr.11.7329.

46. Boiselle PM, Tomico I, Hooley RJ, Pumerantz AS, Selwyn PA, Neklesa VP, et al. Chest radiograph interpretation of Pneumocystis carinii pneumonia, bacterial pneumonia, and pulmonary tuberculosis in HIV-positive patients: accuracy, distinguishing features, and mimics. J Thorac Imaging. 1997;12:47–53, http://dx.doi.org/10.1097/00005382-199701000-00007.

47. Alanoio A, Dellèire S, Voicu S, Bretagne S, Mégabgarne B. The presence of Pneumocystis jirovecii in critically ill patients with COVID-19. J Infect. 2021;82:84–123, http://dx.doi.org/10.1016/j.jinf.2020.10.034.

48. Mauren D, Gayard C, Catherinet E, Givel C, Chabrol A, Tcherakian C, et al. COVID-19 and Pneumocystis jirovecii pneumonia: back to the basics. Respir Med Res. 2021;79:100814, http://dx.doi.org/10.1016/j.jresmer.2021.100814.

49. Setianingrum F, Rauteama-Richardson R, Denning DW. Pulmonary cryptococcosis: a review of pathobiology and clinical aspects. Med Mycol. 2019;57:133–50, http://dx.doi.org/10.1093/mycol/myy086.

50. Hu Z, Chen J, Wang J, Xiong Q, Zhong Y, Yang Y, et al. Radiological characteristics of pulmonary cryptococcosis in HIV-infected patients. PLoS One. 2017;12:e0173858, http://dx.doi.org/10.1371/journal.pone.0173858.

51. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia. 2020;185:599–606, http://dx.doi.org/10.1007/s11046-020-00462-9.

52. Ahmad Sarji S, Wan Abdullah WA, Wistle ML. Imaging features of fungal infection in immuno-suppressed patients in a local ward outbreak. Biomed Imaging Interv J. 2006;2:e21, http://dx.doi.org/10.2349/BIJ.2.2.06.E21.

53. Franquet T, Müller NL, Lee KS, Oikonomou A, Flint JD. Pulmonary candidiasis after hematopoietic stem cell transplantation: thin-section CT findings. Radiology. 2005;236:332–7, http://dx.doi.org/10.1148/radiol.2361031772.
54. Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. Management of coronavirus disease-19 (COVID-19): the Zhejiang experience. Zhejiang Da Xue Xue Bao Yi Xue Ban. 2020;49:147–57, http://dx.doi.org/10.3785/j.issn.1008-9292.2020.02.

55. Agrawal R, Yeldandi A, Savas H, Parekh ND, Lombardi PJ, Hart EM. Pulmonary mucormycosis: risk factors, radiologic findings, and pathologic correlation. Radiographics. 2020;40:656–66, http://dx.doi.org/10.1148/rg.2020190156.