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.

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CT findings of COVID-19-associated pulmonary aspergillosis: a systematic review and individual patient data analysis

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ABSTRACT

Purpose: Common CT abnormalities of pulmonary aspergillosis represent a cavity with air-meniscus sign, nodule, mass, and consolidation having an angio-invasive pattern. This study aims to conduct a systematic review and an individual patient-level image analysis of CT findings of COVID-19-associated pulmonary aspergillosis (CAPA).
Methods: A systematic literature search was conducted to identify studies reporting CT findings of CAPA as of January 7, 2021. We summarized study-level clinical and CT findings of CAPA and collected individual patient CT images by inviting corresponding authors. The CT findings were categorized into four groups: group 1, typical appearance of COVID-19; group 2, indeterminate appearance of COVID-19; group 3, atypical for COVID-19 without cavities; and group 4, atypical for COVID-19 with cavities. In group 2, cases had only minor discrepant findings including solid nodules, isolated airspace consolidation with negligible ground-glass opacities, centrilobular micronodules, bronchial abnormalities, and cavities.
Results: The literature search identified 89 patients from 25 studies, and we collected CT images from 35 CAPA patients (mean age 62.4 ± 14.6 years; 21 men): group 1, thirteen patients (37.1%); group 2, eight patients (22.9%); group 3, six patients (17.1%); and group 4, eight patients (22.9%). Eight of the 14 patients (57.1%) with an atypical appearance had bronchial abnormalities, whereas only one (7.1%) had an angio-invasive fungal pattern. In the study-level analysis, cavities were reported in 12 of 54 patients (22.2%).
Conclusion: CAPA can frequently manifest as COVID-19 pneumonia without common CT abnormalities of pulmonary aspergillosis. If abnormalities exist on CT images, CAPA may frequently accompany bronchial abnormalities.

1. Introduction

Coronavirus disease 2019 (COVID-19) was first reported in December 2019 in Wuhan, China, and became a pandemic shortly thereafter.[1] As a widespread cause of acute respiratory illness, it has resulted in substantial mortality worldwide.[1,2] Superimposed infections of other respiratory pathogens have been a matter of concern since the

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early phase of the COVID-19 pandemic.[3] Bacterial co-infection was found in 7%, on average, of hospitalized patients with COVID-19, which doubled to 14% in intensive care unit patients. Nonetheless, the co-infection rate is lower than has been reported in previous influenza pandemics.[4]

Abbreviations

CAPA	COVID-19-associated pulmonary aspergillosis
CT	Computed tomography
DICOM	Digital Imaging and Communications in Medicine
ECMM	European Confederation for Medical Mycology
ISHAM	International Society for Human and Animal Mycology
GGO	Ground-glass opacities
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Superimposed fungal infections were scarce in early observations,[4] but became increasingly reported as a significant category of superimposed infections posing concerns for an increased risk of mortality, particularly regarding pulmonary aspergillosis in critically ill patients.[1] This novel entity is called COVID-19 associated pulmonary aspergillosis (CAPA), and is similar to influenza-associated pulmonary aspergillosis, which has been found to complicate the course of clinically ill patients with influenza virus.[1,2]

The diagnosis of CAPA can be made based on a combination of histology, microbiology, imaging, and clinical factors,[1] although the diagnostic criteria for CAPA are not standardized.[5] Chest computed tomography (CT) is used as an informative diagnostic tool; however, the understanding of CT findings of CAPA remain limited. Identifying CT findings that suggest the possibility of CAPA infection, as distinct from COVID-19 alone, is a difficult task, especially in patients with conditions that pose infection-control challenges when applying aerosol-generating or invasive diagnostic methods such as bronchoscopy or surgical lung biopsy. Common CT features of pulmonary aspergillosis are generally known as consolidation, nodules, masses, and/or hemorrhagic infarction followed by cavities with air-meniscus sign.[6] However, CT findings of CAPA have not yet been described. Thus, this study aimed to perform a systematic review and an individual patient-level image analysis of the CT findings of CAPA and to investigate radiological features suggestive of co-infection of pulmonary aspergillosis in COVID-19 patients.

2. Materials and methods

This systematic review was performed and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study was approved by Seoul National University Hospital institutional review board (No. H-2106-002-1222). The individual CT images from the participating authors were retrospectively obtained after receiving institutional review board approval with a waiver of patient consent.

2.1. Search strategy

One researcher (S.H.Y., with 9 years of experience in systematic reviews) searched the Embase and OVID-MEDLINE databases to identify all relevant studies that evaluated CAPA with the following search terms: (Coronavirus) OR (COVID 19) OR (SARS-CoV-2) AND (Aspergillosis). Articles published up to January 7, 2021 were included. This search was supplemented by reviewing the bibliographies of the retrieved studies.

2.2. Eligibility criteria for study selection and inclusion of individual patient cases

Two authors (S.H.Y. and W.H.) initially screened the titles and abstracts of all the searched publications using the following inclusion criteria: (a) studies with one or more adult patients with alleged CAPA and (b) studies that conducted a CT scan and reported CT findings of CAPA. We only included case reports, case series, prospective or retrospective cohort studies, letters, not review articles, guidelines, or editorial comments.

After the initial screen, the full-text articles were assessed for eligibility. Any discrepancy between the two authors was harmonized by consensus. The corresponding authors of all eligible studies were contacted via e-mail and asked to share individual anonymized chest CT images of each patient reported in their publications. Cases from the articles with authors who agreed to share CT scans were collected, and we used the individual CT scans in the patient-level analysis. We conducted a study-level analysis of articles where individual CT images could not be shared.

To assemble more cases of individual patients in the patient-level analysis, CAPA cases were surveyed and collected from the members of the Korean Society of Thoracic Radiology along with collecting individual patient CT images from the searched publications. Clinical information and anonymized chest CT images were requested from the members in the same way and included in the patient-level analysis.

2.3. Data extraction

The two authors extracted data from the included studies on study characteristics, including publication year, authors, title, abstract, and number of patients, using a standardized spreadsheet. For the study-level analysis, we collected clinical information and descriptions of the CT findings of CAPA.

In the patient-level analysis, clinical patient data from medical records and anonymized CT scans were collected from the corresponding authors through e-mail. Clinical patient data included age, sex, the underlying disease responsible for immunocompromise, clinical progress of CAPA (days from symptom onset to CAPA diagnosis, days from intensive care unit admission to CAPA diagnosis, the definition of CAPA according to the European Confederation for Medical Mycology (ECMM)/International Society for Human and Animal Mycology (ISHAM) criteria[1] [Supplemental method], the time interval between CAPA diagnosis and CT imaging, the indication of CT imaging), and methods of confirming the diagnosis. Anonymized CT files of patients were collected as encrypted files in either the Digital Imaging and Communications in Medicine (DICOM) format or other image or video file formats such as .jpg or .mov. in a lung window setting (window level, −600; window width, 1500). Most of the participating corresponding authors were not radiologists, so file formats other than DICOM were allowed to facilitate case sharing.

2.4. Image analysis

Two authors (S.H.Y. and W.H. with 16 and 5 years of experience in thoracic radiology, respectively) independently reviewed the CT findings, and joint reading resolved any disagreement. Both readers were blinded to patients' clinical data. According to the Radiology Society of North America expert consensus document reporting language for CT findings related to COVID-19,[7] the CT images were classified as having a typical, indeterminate, or atypical appearance of COVID-19 pneumonia. The images were then initially categorized into one of the following four groups: group 1 (typical appearance), group 2 (indeterminate appearance), group 3 (atypical appearance without cavities nonspecific for superimposed pneumonia), and group 4 (atypical appearance with cavities suspicious for superimposed fungal infections). In group 2, cases had only minor discrepant findings including solid nodules, isolated

airspace consolidation with negligible ground-glass opacities (GGO), centrilobular micronodules, bronchial abnormalities, and cavities. The predominant lung densities were classified as consolidation, GGO, and crazy-paving patterns. The presence of cavitation was reviewed. In cases with an atypical appearance, bronchial lesions and the radiological pattern of pulmonary aspergillosis were assessed as either airway-invasive, angio-invasive aspergillosis, or chronic necrotizing pulmonary aspergillosis.[6,8] The characteristic CT findings of airway-invasive aspergillosis consist of tracheal or bronchial wall thickening and bronchiolitis showing centrilobular nodules and branching areas, while angio-invasive aspergillosis is characterized by nodules surrounded by a halo or pleural-based, wedge-shaped areas of consolidation.[6,8,9] The CT features of chronic necrotizing aspergillosis include unilateral or bilateral segmental areas of consolidation with or without cavitation and multiple nodular areas of increased opacity.[6,8]

In the study-level analysis, the authors reviewed the articles and reported data on clinical patient information, diagnostic methods, and CT findings with representative images. The CT findings were classified into four types, using the same categories as in the patient-level analysis. In addition, we analyzed CT features including cavitation, consolidation, GGO, nodule or mass, cavity, interstitial infiltrates, pleural effusion, and bronchial wall thickening.

2.5. Statistical analysis

We compared patients' clinical characteristics according to the presence of atypical appearance and cavities using the Pearson chi-square test or Fisher exact test for categorical data and the independent *t*-test for continuous data. A *P* value smaller than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Literature search

From the initial literature search identifying 200 publications, after removing duplicate articles ($N = 77$) 123 articles were screened based on title and abstract. Articles in types of review articles, guidelines, and editorial comments ($N = 43$) and those that were not in the field of interest ($N = 27$) were excluded. Then studies without CT image features ($N = 28$) were excluded. Of remaining 25 eligible articles, 7 articles were included in the patient-level analysis as corresponding authors from the publications agreed to share anonymized individual chest CT images and patient data. These 7 articles consisted of 33 patients. Two patients were additionally included from members of the Korean Society of Thoracic Radiology. As a result, a total of 35 patients (mean age, 62.4 ± 14.6 years; 21 men; 33 patients from seven articles[2,10–33] and 2 patients from members of the Korean Society of Thoracic Radiology) were included in the individual patient-level analysis. The other 18 articles were included in the study-level analysis. Total of 89 patients (mean age 64.1 ± 13.0 years; 53 men) from 25 studies and the Korean Society of Thoracic Radiology members were included in this study[2,10–33] (Fig. 1).

3.2. Clinical characteristics of the patient-level analysis

The baseline clinical characteristics of the 35 patients included in the patient-level analysis are presented in Table 1. Twenty-three patients (65.7%) were classified as having probable CAPA according to the ECMM/ISHAM criteria[1] and 12 patients (34.3%) as having possible CAPA. Eleven patients (31.4%) did not have immunocompromising condition, but 24 patients (68.6%) had underlying conditions causing immunocompromise. The most common cause was a history of steroid treatment consisting of 19 patients (54.3%) followed by use of tocilizumab (4 patients, 11.4%), leukemia (5 patients, 14.3%), and lung transplantation (2 patients, 5.7%). Six patients had overlapping conditions.

3.3. CT Findings of CAPA: patient-level analysis

Table 2 summarizes the CT findings of CAPA in the patient-level analysis. Thirteen patients (37.1%) showed a typical appearance of COVID-19 pneumonia. Eight patients (22.9%) had an indeterminate appearance. The discrepant findings consisted of small pure solid nodules (5 patients), isolated patchy consolidations without GGO (2 patients), small isolated cavities (2 patients), and centrilobular micronodules (1 patient). Six patients (17.1%) had an atypical appearance without cavities nonspecific for superimposed pneumonia (Figs. 2, 3), and eight patients (22.9%) had an atypical appearance with cavities suspicious for superimposed fungal infections (Figs. 4, 5). Among the 14

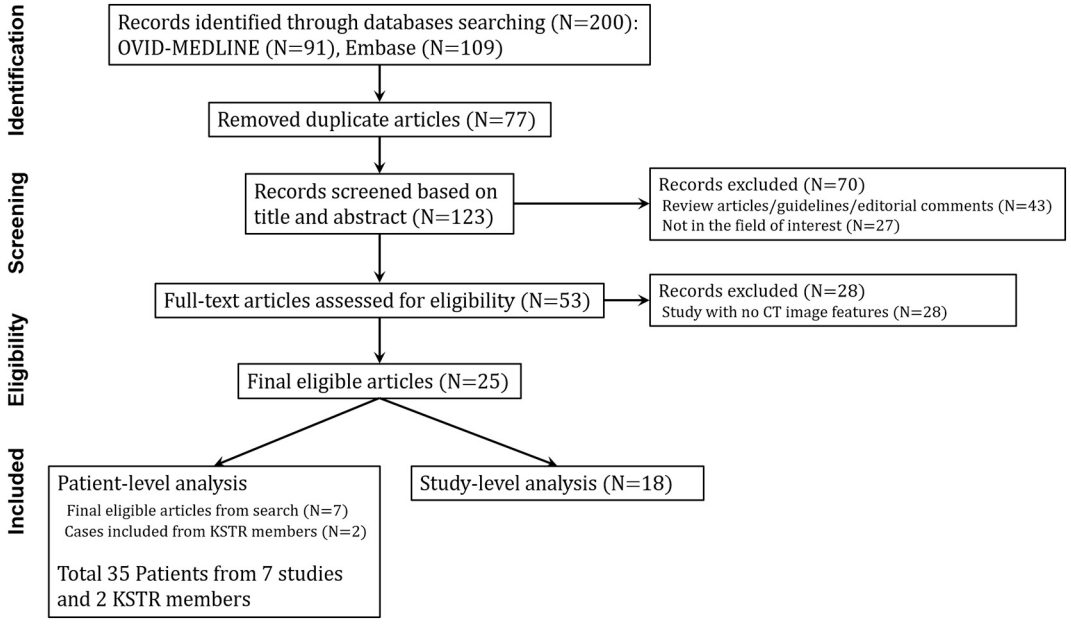

Fig. 1. Flow diagram of the literature search.

Table 1
Clinical characteristics of patients with CAPA in the individual patient-level image analysis.

Age (years, average ± standard deviation)	62.4 ± 14.6 (range, 23–94)
Sex (men)	21 (60.0%)
Definition of CAPA according to the 2020 ECMM/ISHAM consensus criteria	
Probable CAPA	23 (65.7%)
Possible CAPA	12 (34.3%)
Underlying disease[a]	
None	9 (25.7%)
Hypertension	11 (31.4%)
Diabetes mellitus	5 (14.3%)
Leukemia	5 (14.3%)
Cardiomyopathy or cardiac disease	3 (8.6%)
Chronic obstructive pulmonary disease	3 (8.6%)
Lung transplantation	2 (5.7%)
Hepatitis B	4 (11.4%)
Essential thrombocythaemia	1 (2.9%)
Underlying immunocompromising condition[a]	
None	11 (31.4%)
Steroids	19 (54.3%)
Toclizumab	4 (11.4%)
Leukemia	5 (14.3%)
Lung transplantation	2 (5.7%)
Median days from symptom onset to CAPA diagnosis[b]	11.5 days (7/18.3)
Median days from ICU admission to CAPA diagnosis[b]	6 days (1.5/12.5)
Median time interval between CAPA diagnosis and CT imaging[b]	1 days (−3.3/7.3)
Indication of diagnostic CT imaging for CAPA	
Fever	11 (31.4%)
Higher oxygen demands and acute respiratory distress syndrome	26 (74.3%)
Radiologic deterioration	3 (8.6%)

CAPA = COVID-19-associated pulmonary aspergillosis.
[a] Data are number of each category. Patients may have overlapping diseases.
[b] Data in parenthesis indicates interquartile ranges.

Table 2
Per-patient CT findings of COVID-19-associated pulmonary aspergillosis: individual patient-level image analysis.

	Number of case (%)
COVID-19 lesions on CT images[a]	
Group 1, typical appearance	13 (37.1)
Group 2, indeterminate appearance	8 (22.9)
Group 3, atypical appearance without cavities	6 (17.1)
Group 4, atypical appearance with cavities	8 (22.9)
Dominant lung densities	
Consolidation	15 (42.9)
Ground glass opacities	10 (28.6)
Crazy-paving	10 (28.6)
Cavitation	
Present	10 (28.6)
Absent	25 (71.4)
Total	35 (100.0)

[a] The CT findings were categorized as having a typical, indeterminate, or atypical appearance based on the Radiological Society of North America expert consensus and further divided into four groups.

patients with an atypical appearance, bronchial abnormalities existed in 57.1% (8/14) of atypical appearance, representing the airway-invasive aspergillosis pattern, whereas only one case of atypical appearance (7.1%, 1/14) had an angio-invasive aspergillosis pattern and chronic necrotizing pulmonary aspergillosis, respectively. Four cases had non-classifiable pulmonary aspergillosis patterns. Cavitation was found in 28.6% (10/35) (Table 2).

Table 3 represents a per-lesion analysis of chest CT findings not explained by COVID-19 pneumonia, including cavity, solid nodule, bronchial wall thickening, centrilobular nodules, and consolidation

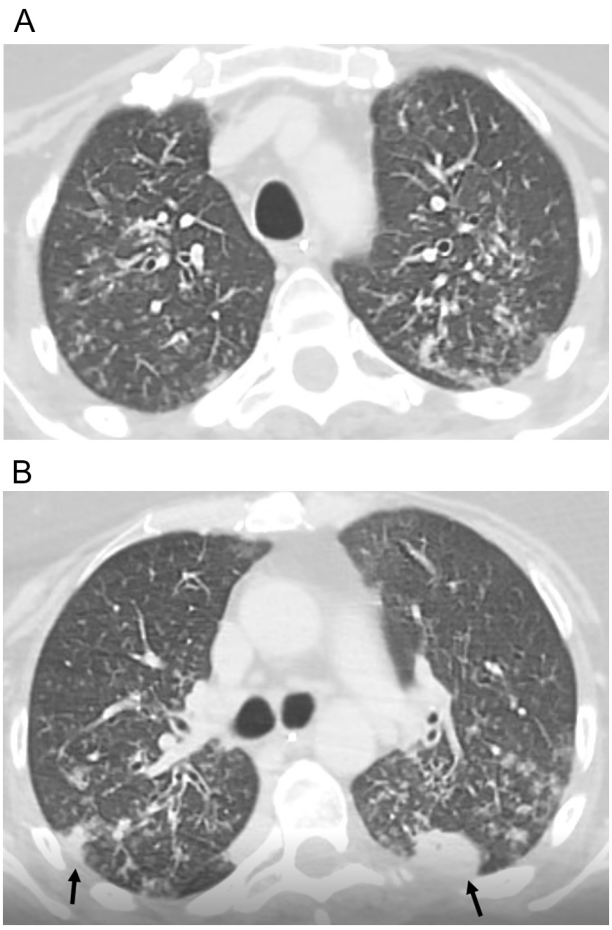

Fig. 2. Axial CT images in a 53-year-old female patient with a diagnosis of probable COVID-19-associated pulmonary aspergillosis and atypical CT appearance for COVID-19 without cavities. CT images show centrilobular micronodules with bronchial wall thickening in both upper lobes (A–B). Subpleural nodules and subpleural nodular consolidations without ground-glass opacities (arrows) are also noted (B).

without GGO. Among the 55 cavity lesions in 10 patients, 74.5% were located in the upper lobes, and 81.8% were smaller than 3 cm (Table 3, Figs. 4, 5). A bronchovascular distribution was present in 63.6% of lesions, and 80% of cavities had thick walls defined as >2 mm. For solid nodules, 75% were located in the upper lobes, and 90.4% had well-defined margins. Bronchovascular, nonsubpleural distribution was predominant (84.6% and 57.7, respectively). Halo sign was noted in 5.8% (Table 3).

3.4. CT findings of CAPA: study-level analysis

The study-level analysis of the CT findings of CAPA is summarized in Tables 4 and S1. Eighteen studies were included in the study-level analysis, and 92 patients were diagnosed as having CAPA. Description or images of CT features were available for 54 patients.

According to the pattern classification, 20 cases (37.0%) showed a typical appearance of COVID-19 pneumonia, and 7 cases (13.0%) had an indeterminate appearance. Seven patients (13.0%) showed an atypical appearance without cavities, while 22.2% (12/54) had an atypical appearance with cavities.

In the 54 cases of CAPA, the most common imaging finding was GGO, present in 85.2% of cases (46/54), followed by consolidations (36 cases, 66.7%). A nodule or mass was observed in 9 cases (16.7%), and cavities were present in 22.2% (12/54).

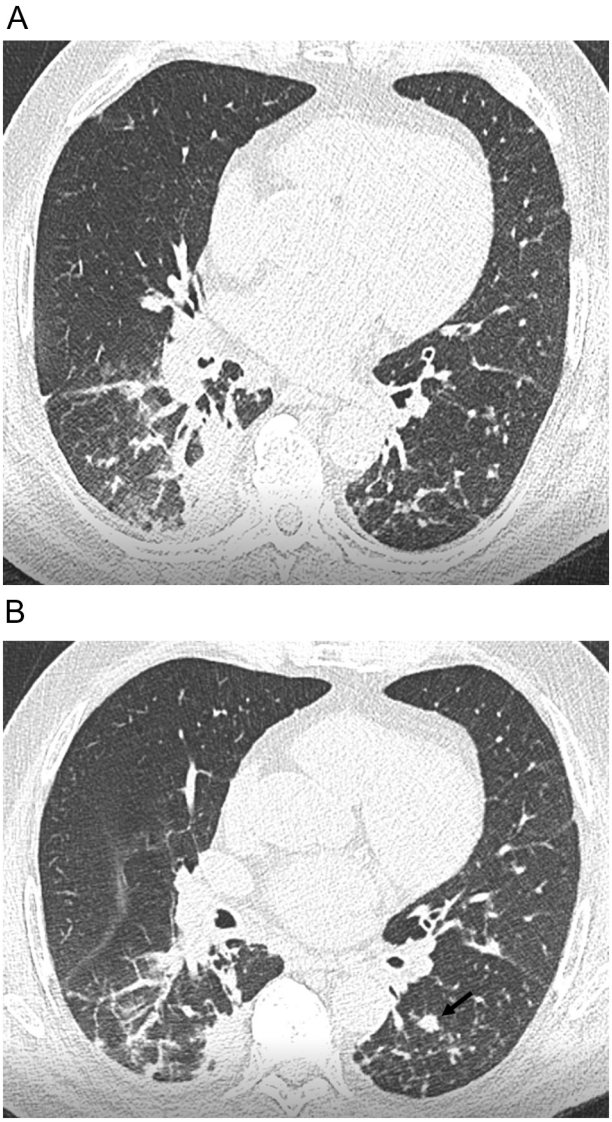

Fig. 3. Axial CT images in a 69-year-old male patient with a diagnosis of probable COVID-19-associated pulmonary aspergillosis and atypical CT appearance for COVID-19 without cavities. CT images show subpleural consolidation without ground-glass opacities and multiple lobar and segmental bronchial wall thickening in the right lower lobe (A). A well-defined round solid nodule without a halo (arrow) and a few centrilobular micronodules are present in the left lower lobe (B).

3.5. Relationship of CT findings with patient characteristics

In the analyses of the relationship of CT findings with patient characteristics, no significant differences were found according to the presence of an atypical appearance and cavities (Table S2).

4. Discussion

The strength of this study is that it comprehensively analyzed the CT features of CAPA by reviewing individual patient-level data and confirmed the features through a systematic search of the literature. We investigated that about 37% of CAPA patients had typical appearance for COVID-19 on CT in both patient-level and study-level analyses. This study also revealed that 40.0% (14/35) of CAPA cases had an atypical appearance for COVID-19 on CT images in the individual patient-level analysis, and we confirmed a similar proportion of atypical appearances (35.2%; 19/54) in the study-level analysis. Cavities were observed

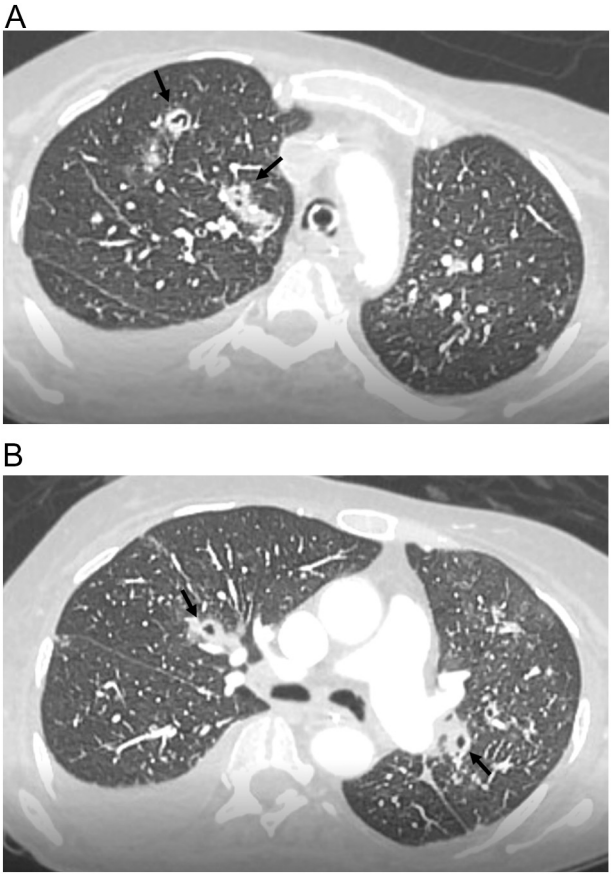

Fig. 4. Axial CT images in a 48-year-old female patient diagnosed with probable COVID-19-associated pulmonary aspergillosis and atypical CT appearance for COVID-19 with cavities. CT images shows multiple cavities smaller than 3 cm (arrows) in both upper lobes (A–B). Cavities show thick irregular walls and nonsubpleural bronchovascular distribution (A–B). Air-crescent sign is present in the one of the cavities in the right upper lobe (A).

in about one-fifth of CAPA patients in both analyses. An atypical appearance and cavities tended to be more common in immunocompromised patients, although this tendency was not statistically significant. Among the patients with an atypical appearance, CAPA frequently accompanied bronchial abnormalities as a unique manifestation of invasive aspergillosis in COVID-19,[34] whereas an angio-invasive aspergillosis pattern was rare.

Common features not explained by COVID-19 in individual patient-level CAPA images consisted of cavities, pure solid nodules, consolidation without GGO, bronchial wall thickening, and centrilobular nodules. Among these, cavities and pure solid nodules (potentially representing aspergilloma[35]) were predominant, and they were primarily found in the upper lobes (74.5% and 75%, respectively). They were frequently distributed along nonsubpleural bronchovascular bundles. Conventional perilesional CT features of invasive pulmonary aspergillosis, such as the halo sign or reversed halo sign, were unevaluable in some cases due to the underlying GGO of COVID-19 pneumonia, and even in areas without GGO, the halo sign, reversed halo sign, and air-meniscus sign were infrequent in CAPA compared to typical angio-invasive pulmonary aspergillosis.[36] These signs are time-dependent signs of angio-invasive aspergillosis pattern. There is a possibility that in the early stage of fungal infection, nonspecific findings such as small solid nodules may have appeared without these representing signs. This might partly explain the low number of the typical angio-invasive patterns.

Interestingly, whereas invasive pulmonary aspergillosis more frequently shows an angio-invasive pattern than an airway-invasive pattern in immunocompromised patients, CAPA showed the opposite

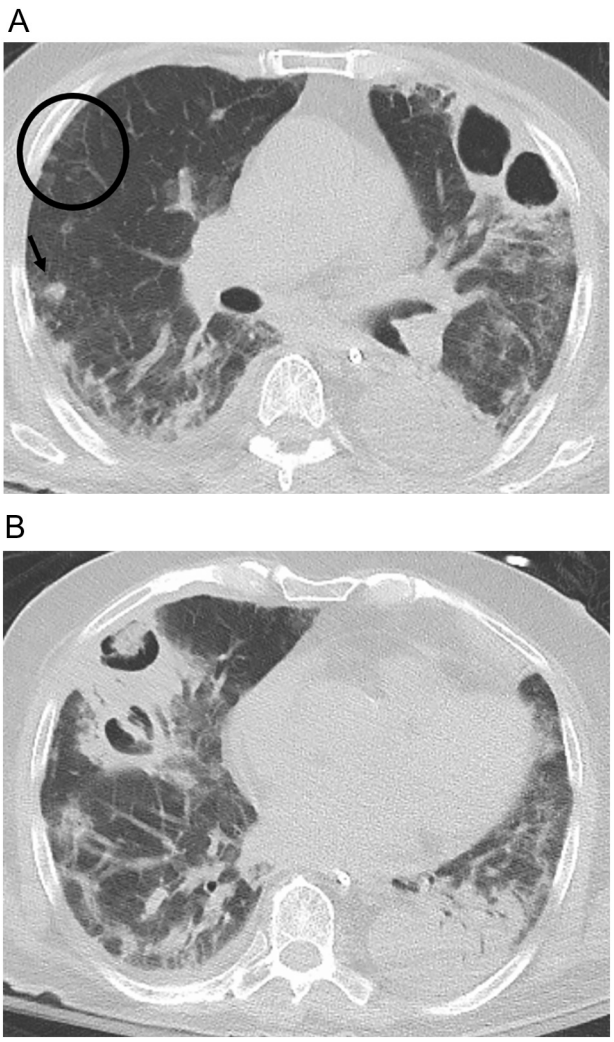

Fig. 5. Axial CT images in a 73-year-old male patient diagnosed with probable COVID-19-associated pulmonary aspergillosis and atypical CT appearance for COVID-19 with cavities. CT images show multiple large cavities with thick irregular or smooth walls in the left upper and right middle lobes (A–B). Debris exist in the cavities of the right middle lobe. Poorly defined solid nodules (arrow) and centrilobular nodules (within circle) are noted in the right upper lobe (A).

predilection, with an airway-invasive pattern in 57.1% of patients and an angio-invasive pattern in only 7.1%. This could possibly be caused by colonies of *Aspergillus* spreading through the airways, implanting fungus and growing colonies into microscopically destructed or dilated bronchi of lungs that were infected with COVID-19,[8,35] rather than vascular invasion and occlusion of small to medium-sized pulmonary arteries by fungal hyphae forming hemorrhagic nodules on CT.[6] Bronchial predilection of CAPA was supported by the paucity of halo and reversed halo signs on CT reflecting pulmonary infarction due to fungal angioinvasion. In line with our findings, a recent histopathologic analysis showed tracheal ulceration and superficial tissue invasion by hyphae while there was no evidence of angioinvasion in patients with invasive *Aspergillus* tracheobronchitis in patients and COVID-19.[34] They suggest that the ability of *Aspergillus* to cause angioinvasion is hypothesized as a crucial step, so-called angioinvasion threshold model.[34] According to this model, the aggregation of factors that contribute to disease progression of invasive *Aspergillus* tracheobronchitis ultimately leads to angionvasion, and invasive *Aspergillus* tracheobronchitis in a case of influenza typically surpasses the angioinvasion threshold, while CAPA remains to have tissue invasion without less likely surpassing angioinvasion.[34]

Cavitation is not known as a common feature of COVID-19 pneumonia.[7] When cavitation appears on CT in patients with COVID-19 pneumonia, other possibilities should be considered. The differential diagnoses are superimposed infection including aspergillosis, actinomycosis, nocardiosis or other rare infections, pulmonary tuberculosis, and septic pulmonary emboli. In rare cases with initial CT without significant signs of co-infection, unidentified underlying disease such as vasculitis or malignancy should be reviewed.

Despite recent revealing studies on the definition and diagnosis of CAPA, the diagnosis of CAPA still remains challenging,[1,5,10,19,37,38] especially in critically ill or mechanically ventilated patients in whom fungal infections frequently occur. For this reason, the prevalence of CAPA has been variously reported among studies according to definitions and surveillance practices.[39] In this study, we classified CAPA patients according to the ECMM/ISHAM criteria as having proven, probable, or possible CAPA, which is defined based on histologic, microbiologic, imaging, and clinical factors.[1] These definitions are highly reliant on bronchoscopy, and in many patients with COVID-19, performing bronchoscopy and obtaining bronchoalveolar lavage fluid is challenging. In addition, the cut-off values for biomarkers such as Galactomannan assays performed in serum and/or bronchoalveolar lavage fluid have not been validated.[40] The role of imaging in CAPA is also not well established due to the lack of recognized CT features of CAPA and potential overlapping findings between aspergillosis and COVID-19 pneumonia.[1] Our study suggests that CT, as a noninvasive diagnostic tool, can play a salient role by suggesting the possibility of superimposed infection and depicting cavities in a particular proportion of patients suspected to have CAPA. If CT findings are inconsistent with typical appearance of COVID-19 and especially if cavities or bronchial abnormalities are found, it is an important role as a radiologist to provide a differential diagnosis for co-infection of aspergillosis.

This study has several limitations. First, the number of included studies was relatively small. Second, CT images were collected through e-mail in various file formats, including DICOM and non-DICOM images or video clips of stacked CT images; accordingly, the quality of the collected CT images was inconsistent. Nevertheless, all the collected CT images were acceptable for image analysis. Third, there was limited information about the diagnostic methods of CAPA and sampling specimens in some patients. Fourth, the study-level image analysis was based on the texts of the published articles, which might have limitations in identifying minor discrepant findings in cases with a typical/indeterminate appearance for COVID-19 (individual patient-level analysis, 20.0%; study-level analysis, 5.6%). Fifth, we assessed the diagnostic discernability of CAPA based on the 2020 ECMM/ISHAM consensus criteria rather than a quality assessment of participated studies as the studies format varied from cohort studies to a single case report. Lastly, the possible reason why airway-invasive patterns were predominant in our study might be because the ECMM/ISHAM criteria were defined highly reliant on bronchoscopy.

5. Conclusions

In conclusion, approximately one-third of patients with CAPA had an atypical appearance for COVID-19, and cavities were observed in one-fifth of the patients. Among the atypical appearances, the airway-invasive pattern with bronchial abnormalities was frequently present, while the angio-invasive pattern was rare. For an appropriate CAPA diagnosis, it will be helpful to recognize that a considerable proportion of CAPA cases can manifest without a radiologic suspicion of superimposed infection on CT scans with a typical or indeterminate appearance for COVID-19. If abnormalities exist on CT images, CAPA may frequently accompany bronchial abnormalities with or without cavities. These findings of our study were infrequently reported for radiologic features of pulmonary aspergillosis. By understanding this unique manifestation of CAPA, radiologists will be able interpret CT images properly in COVID-19 patients when CAPA is clinically suspected.

Table 3
Per-lesion CT findings of COVID-19-associated pulmonary aspergillosis: individual patient-level image analysis.

Cavity ($N = 55$)	N (%)	Solid nodule ($N = 52$)	N (%)	Other findings	N (%)
Lobar location		Lobar location		Bronchial wall thickening ($N = 15$)	
Right upper lobe	22 (40.0)	Right upper lobe	31 (59.6)	Bilateral	6 (40.0)
Right middle lobe	7 (12.7)	Right middle lobe	5 (9.6)	Unilateral	9 (60.0)
Right lower lobe	6 (10.9)	Right lower lobe	5 (9.6)	Lobar	5 (33.3)
Left upper lobe	19 (34.5)	Left upper lobe	8 (15.4)	Segmental	10 (66.7)
Left lower lobe	1 (1.8)	Left lower lobe	3 (5.8)		
Size		Margin		Centrilobular micronodules ($N = 12$)	
<3 cm	45 (81.8)	Well	47 (90.4)	Upper lobes	8 (66.7)
3–5 cm	6 (10.9)	Ill	5 (9.6)	Lower lobes	4 (33.3)
>5 cm	4 (7.3)	Location			
Location		Subpleural	22 (42.3)	Subpleural patchy consolidation without ground-glass opacities ($N = 13$)	
Subpleural	24 (43.6)	Nonsubpleural	30 (57.7)	Upper lobes	2 (15.4)
Nonsubpleural	31 (56.4)	Distribution		Lower lobes	11 (84.6)
Distribution		Bronchovascular	44 (84.6)		
Bronchovascular	35 (63.6)	Nonbronchovascular	8 (15.4)	Nonsubpleural patchy consolidation without ground-glass opacities (N = 4)	
Nonbronchovascular	20 (36.4)	Shape		Lower lobes	4 (100.0)
Wall		Round	29 (55.8)		
Thick	44 (80.0)	Elongated/oval	6 (11.5)		
Thin	11 (20.0)	Irregular	17 (32.7)		
Smooth	26 (47.3)	Halo			
Irregular	29 (52.7)	Yes	3 (5.8)		
Septa		No	42 (80.8)		
Present	16 (29.1)	Unevaluable[a]	7 (13.5)		
Absent	39 (70.9)				
Debris					
Present	11 (20.0)				
Absent	44 (80.0)				
Crescent sign	4 (7.3)				

Data in parenthesis indicates percentage.
[a] The presence of a halo sign could not be evaluated due to ground-glass opacities surrounding the nodules.

Table 4
CT findings of COVID-19-associated pulmonary aspergillosis: study-level analysis based on the text.

COVID-19 lesions on CT images[a]	Number of cases (%)
Group 1, typical appearance	20 (37.0)
Group 2, indeterminate appearance	7 (13.0)
Group 3, atypical appearance without cavities	7 (13.0)
Group 4, atypical appearance with cavities	12 (22.2)
Unknown	8 (14.8)
Total	54

Individual CT findings	Number of cases (%)
Consolidation	36/54 (66.7)
Ground glass opacities	46/54 (85.2)
Nodule or mass	9/54 (16.7)
Cavity	12/54 (22.2)
Interstitial infiltrates	5/54 (9.3)
Pleural effusion	3/54 (5.6)
Bronchial wall thickening	4/54 (7.4)
Pulmonary embolism	6/54 (11.1)
Reversed halo	1/54 (1.9)

Data in parenthesis indicates percentage.
[a] The CT findings were categorized as having a typical, indeterminate, or atypical appearance based on the Radiological Society of North America expert consensus and further divided into four groups.

Furthermore, developing new imaging approach (i.e., deep learning) beyond visual analysis is urged for a timely imaging diagnosis of superinfection in this and future pandemic.

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Declaration of competing interest

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Supplementary data

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