INTRODUCTION

With the emergence of the COVID-19 pandemic, there have been a number of reports worldwide of COVID-19-associated pulmonary aspergillosis (CAPA).\(^1\)\(^-\)\(^3\) As observed in influenza-associated pulmonary aspergillosis, patients with CAPA may lack classic host factors for invasive fungal diseases.\(^4\) It is speculated that immune dysregulation associated with acute respiratory distress syndrome (ARDS), disrupted ciliary clearance and lymphopenia due to severe respiratory viral infection may contribute to the development of invasive pulmonary aspergillosis in critically ill patients with COVID-19.\(^5\)\(^,\)\(^6\) Multiple prospective cohort studies suggested that CAPA was associated with increased mortality in patients with COVID-19.\(^7\)\(^-\)\(^{12}\) Furthermore, corticosteroids are currently being used to patients with severe COVID-19 more universally than in early 2020 since RECOVERY trial\(^13\) showed mortality benefit, which could lead to a further increase in the incidence of CAPA in the ICU. Galactomannan testing from bronchoalveolar lavage (BAL) fluid is the most sensitive test for pulmonary aspergillosis in ICU patients;\(^6\) however, studies on CAPA have been hindered by diagnostic challenges, primarily as
bronchoscopies are rarely performed in patients with COVID-19 due to the risk of disease transmission. As the majority of studies on CAPA have been case series, and small observational studies, the true incidence and clinical significance of CAPA in ICU patients is uncertain. In this study, we conducted a systematic review and meta-analysis to determine the incidence and mortality of CAPA in patients with COVID-19 for better guidance on surveillance and prognostication.

2 | PATIENTS AND METHODS

2.1 | Data sources and search

All prospective and retrospective observational studies reporting CAPA were searched using a two-level search strategy. First, we conducted a comprehensive literature search of PubMed and Embase databases through 4 April 2021. The search terms included (“COVID-19” OR “SARS-CoV-2” OR “coronavirus”) AND (“aspergillosis” OR “aspergillus”). Second, we performed an additional manual search of secondary sources, including references of initially identified articles, to maximise the completeness of the collection of relevant studies. The search was performed without language restriction.

2.2 | Study selection

A study was included in the meta-analysis if the following criteria were met: (1) the study was published in a peer-reviewed journal, (2) the study design was a prospective or retrospective observational study, (3) the study population included hospitalised adult patients with COVID-19 and (4) the diagnosis of pulmonary aspergillosis was made based on specific case definitions or diagnostic algorithms including the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) definitions, modified AspICU algorithm, case definitions of influenza-associated pulmonary aspergillosis (IAPA), and the European Confederation for Medical Mycology and the International Society for Human and Animal Mycology (ECMM/ISHAM) consensus criteria. We excluded observational studies with diagnostic criteria and assessed the eligibility of each study. The full text of articles was retrieved for eligibility assessment and further analyses after the initial screening with title and abstract. Any discrepancies were resolved by discussion and consensus. The following data were extracted from each eligible study: author name, study location, design, setting and case definition or diagnostic algorithm used to classify CAPA. We also collected the following patient characteristics and outcomes: the number of patients in the ICU during the study period, the number of patients with CAPA, the numbers of patients who received systemic steroids, tocilizumab and antifungal treatment, and the number of deaths among the patients with CAPA. If the patient population in a primary study was not limited to the ICU, we used only patients in the ICU for the analysis.

2.4 | Statistical analysis

The endpoints of this study were the incidence and mortality of CAPA in patients with COVID-19 in the ICU. We conducted a one-group meta-analysis with a random-effects model using the DerSimonian-Laird method. OpenMetaAnalyst version 12.11.14 was used to perform the statistical analysis (available at http://www.cebm.brown.edu/openmeta/). The I² statistic was used to quantify heterogeneity among studies, with I² > 50% indicating substantial heterogeneity. This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

3 | RESULTS

A total of 302 articles were identified through the initial database search and subsequent manual search. After the removal of duplicated items and screening based on title and abstract, 105 articles were assessed for eligibility. We excluded 77 articles including five case series and 38 case reports. Notably, two retrospective observational studies were excluded because the case definitions or diagnostic algorithms used to classify pulmonary aspergillosis were not documented. Finally, 28 observational studies were included in our meta-analysis (Figure 1).

The study characteristics included in the meta-analysis are summarised in Table 1. Among the 28 studies selected, 23 were conducted in European countries, two in Mexico and one each in China, Pakistan and the United States. All studies started during the first wave of the pandemic, or in early 2020, with the exception of four studies that did not specify their study periods. Routine screening for secondary invasive fungal infection (eg aspergillosis and candidiasis) was employed in 13 studies. There was a variation in galactomannan index cut-off values used across studies. For serum galactomannan index, 0.5 was the most common cut-off value, used by 16 studies, followed by 1.0 being used by two studies. For BAL galactomannan index, 1.0 was most commonly used by 16 studies, followed by 0.5 and 0.8 being used by two studies, respectively. Five studies did not document the
cut-off values for galactomannan index. The modified AspICU algorithm was used in 15 studies and was the most commonly used case definition and diagnostic algorithm. The median age ranged from 55 to 70. The percentage of males ranged from 60% to 82%. Median time from ICU admission to the diagnosis of CAPA ranged from 3 to 15 days. There was a large variation between studies in the percentages of patients with CAPA receiving systemic steroids and antifungal treatment, ranging from 0% to 100% and 22 to 100%, respectively. A total of 3148 patients with COVID-19 in the ICU were included in the analysis. The incidence and mortality of CAPA in the ICU were estimated to be 10.2% (95% CI, 8.0–12.5; \(I^2 = 82.0\%\)) and 54.9% (95% CI, 45.6–64.2; \(I^2 = 62.7\%\)), respectively (Figures 2 and 3).

4 | DISCUSSION

In this meta-analysis, we estimated the incidence and mortality of CAPA in critically ill patients with COVID-19 in the ICU. CAPA occurred in 10.2% of cases in these studies and was associated with high mortality. Since the start of the COVID-19 pandemic, CAPA has been reported as a complication of mechanically ventilated patients with COVID-19 from across the world. However, epidemiological data on incidence and mortality were variable as the reports were mainly based on case series and small observational studies, especially in the early stages of the pandemic.

Early studies and case series from Europe reported that pulmonary aspergillosis occurred in 20%-35% of cases in the ICU.\(^1\)-\(^3\),\(^18\),\(^33\) However, several more recent prospective cohort studies reported a lower incidence of 3%.\(^11\),\(^12\) Interestingly, studies with larger sample sizes had lower estimates of incidence, potentially suggesting reporting bias in smaller studies. Given that as many as about 10% of mechanically ventilated patients with COVID-19 in the ICU were affected by CAPA as shown in our analysis, routine surveillance with tracheal aspirate and non-bronchoscopic lavage, serum galactomannan and chest CT might be justified.\(^5\) This high incidence, combined with considerable mortality, might also increase the need for clinical trials to determine whether antifungal prophylaxis is beneficial. The high heterogeneity in incidence among each study may be explained by the differences in (1) the routine screening for CAPA, (2) the case definitions used and (3) the pharmacological treatment of critically ill patients with COVID-19. First, there may be a risk of overdiagnosis with routine BAL in mechanically ventilated patients with COVID-19 since positive mycological BAL testing can lead to the classification of CAPA, while progressive radiological and clinical manifestations of COVID-19 itself may fulfill these criteria. Salmont-García and colleagues also suggested that practice variations in screening for CAPA in COVID-19 patients might have affected detection rates.\(^3\) Second, it is possible that heterogeneous conditions, including colonisation with Aspergillus, were reported as CAPA because the definition of CAPA was not clearly determined until recently.\(^5\) It is highly likely that there is underdiagnosis in studies using only EORTC/MSG definitions that are unsuitable for patients in ICU, as a number of patients may not be classifiable due to a lack of host factors and typical radiological features.\(^20\) Underdiagnosis might also be present with the original and modified AspICU criteria since they do not include PCR testing, which is incorporated into the new case definitions and would lead to increased case detection rates. Several studies that examined multiple diagnostic criteria simultaneously found differences in the number of patients classified.\(^7\),\(^8\),\(^30\) Third, many of the studies included in the meta-analysis were conducted before treatment standardisation where pharmacologic therapies
**TABLE 1** Study and patient characteristics

| Author              | Country        | Design        | Setting         | Study period                  | Population                        | Routine screening for aspergillosis |
|---------------------|----------------|---------------|-----------------|-------------------------------|-----------------------------------|------------------------------------|
| Alanio et al        | France         | Prospective   | Single-centre   | -                             | MV patients in the ICU            | Yes                                |
| Bartoletti et al    | Italy          | Prospective   | Multicentre     | Feb 22–Apr 20, 2020           | MV patients in the ICU            | Yes                                |
| Chauvet et al       | France         | Retrospective | Single-centre   | Mar 24–May 25, 2020           | ARDS patients in the ICU          | No                                 |
| Dellièrè et al      | France         | Retrospective | Multicentre     | Mar 15–May 01, 2020           | Patients in the ICU               | No                                 |
| Dupont et al        | France         | Prospective   | Multicentre     | Mar 01–Apr 11, 2020           | Patients in the ICU               | No                                 |
| Fekkar et al        | France         | Retrospective | Single-centre   | Mar 6–Apr 24, 2020            | Patients in the ICU               | No                                 |
| Gangneux et al      | France         | Prospective   | Single-centre   | -                             | MV patients in the ICU            | Yes                                |
| Gouzien et al       | France         | Retrospective | Single-centre   | Mar 01–Apr 30, 2020           | Patients in the ICU               | Yes                                |
| Koehler et al       | Germany        | Retrospective | Single-centre   | Mar 07–Apr 22, 2020           | ARDS patients in the ICU          | Yes                                |
| Lahmer et al        | Germany        | Prospective   | Single-centre   | Mar 01–Apr 30, 2020           | MV patients in the ICU            | Yes                                |
| Lamoth et al        | Switzerland    | Retrospective | Single-centre   | Mar 06–May 11, 2020           | MV patients in the ICU            | Yes                                |
| Machado et al       | Spain          | Prospective   | Single-centre   | Mar 01–May 31, 2020           | All hospitalised patients         | No                                 |
| Maes et al          | UK             | Retrospective | Single-centre   | Mar 15–Aug 30, 2020           | MV patients in the ICU            | No                                 |
| Nasir et al         | Pakistan       | Retrospective | Single-centre   | Feb–Apr, 2020 (Date unspecified) | All hospitalised patients         | No                                 |
| Permpalung et al    | USA            | Retrospective | Multicentre     | Mar–Aug, 2020 (Date unspecified) | MV patients in the ICU            | Yes                                |
| Razazi et al        | France         | Retrospective | Single-centre   | Oct 01, 2009–Apr 29, 2020     | MV patients in the ICU            | No                                 |
| Ripa et al          | Italy          | Prospective   | Single-centre   | Feb 25–Apr 06, 2020           | All hospitalised patients         | No                                 |
| Roman-Montes et al  | Mexico         | Retrospective | Single-centre   | Apr 13–Jun 01, 2020           | MV patients in the ICU            | No                                 |
| Rutsaert et al      | Belgium        | Retrospective | Single-centre   | Mar 12–Apr 25, 2020           | MV patients in the ICU            | No                                 |
| Sarrazyn et al      | Belgium        | Retrospective | Single-centre   | Mar 11–Apr 17, 2020           | All hospitalised patients         | Yes                                |
| Segrelles-Calvo et al | Spain       | Prospective   | Single-centre   | Feb 01–Apr 30, 2020           | Patients in the ICU               | Yes                                |
| van Arkel et al     | Netherlands    | Retrospective | Single-centre   | -                             | MV patients in the ICU            | No                                 |
| Van Biesen et al    | Netherlands    | Retrospective | Single-centre   | -                             | MV patients in the ICU            | Yes                                |
| van Grootveld et al | Netherlands    | Retrospective | Single-centre   | Apr 01–May 11, 2020           | Patients in the ICU               | Yes                                |
| Vélez Pintado et al | Mexico         | Retrospective | Single-centre   | Mar 15–Jul 10, 2020           | Patients in the ICU               | No                                 |
| Versyck et al       | France         | Retrospective | Single-centre   | Mar 15–Apr 30, 2020           | MV patients with in the ICU       | Yes                                |
| Wang et al          | China          | Retrospective | Single-centre   | Jan–Mar, 2020 (Date unspecified) | All hospitalised patients         | No                                 |
| White et al         | UK             | Prospective   | Multicentre     | -                             | Patients in the ICU               | No                                 |

**Author** | **Patients with COVID-19 in the ICU** | **Patients with CAPA** | **Days from COVID-19 diagnosis** | **Days from ICU admission**
---|---|---|---|---|
Alanio et al | 27 | 9 | - | - |
Bartoletti et al | 108 | 30 | - | - |
Chauvet et al | 46 | 6 | - | - |
Dellièrè et al | 366 | 21 | - | 6 (1–15) |
Dupont et al | 106 | 19 | 11 (7–14) | 10 (8–14.5) |
Fekkar et al | 260 | 6 | - | 7 (2–56) |
Gangneux et al | 45 | 7 | - | - |
Gouzien et al | 53 | 2 | - | - |
Koehler et al | 19 | 5 | - | - |
Lahmer et al | 32 | 11 | - | 4 (range, 1–7) |
Lamoth et al | 80 | 3 | 8 (7–13) | 7 (3–8) |

**Note:** The table continues on the next page.
| Case definition/diagnostic algorithm | Age            | Male (%) | Hypertension (%) | Diabetes (%) | Obesity (%) | CKD (%) | COPD (%) | Immunosuppressive condition (%) |
|-------------------------------------|----------------|----------|------------------|--------------|-------------|---------|----------|--------------------------------|
| Modified AspICU                     | 63 (56–71)     | 67       | –                | –            | –           | –       | –        | –                              |
| AspICU, IAPA                        | 63 (57–70)     | –        | 63               | 17           | 43          | 12      | 17       | –                              |
| EORTC/MSG, AspICU, modified AspICU | –              | –        | –                | 41           | 72          | –       | 13       | 11                             |
| EORTC/MSG, IAPA                     | 62 (56–68)     | 82       | 59               | 37           | 32          | –       | 2        | 9                              |
| Modified AspICU                     | –              | –        | –                | –            | –           | –       | –        | –                              |
| EORTC/MSG, modified AspICU          | –              | –        | –                | –            | –           | –       | –        | –                              |
| Modified AspICU                     | 55 (48–64)     | 72       | 57               | 32           | 68          | –       | 6        | 14                             |
| AspICU, modified AspICU             | 60 (53–71)     | 71       | 33               | 38           | –           | 9       | 0        | –                              |
| EORTC/MSG, AspICU, modified AspICU | 64 (55–74)     | 68       | 43               | 25           | 34          | –       | 13       | –                              |
| AspICU, modified AspICU             | –              | –        | –                | –            | –           | –       | –        | –                              |
| Modified AspICU                     | 70 (range, 27–84) | 72      | 65               | 25           | –           | 16      | 10       | –                              |
| IAPA                                | –              | –        | –                | –            | –           | –       | –        | –                              |
| EORTC/MSG, modified AspICU          | –              | –        | –                | –            | –           | –       | –        | –                              |
| Modified AspICU                     | 62 (50–70)     | 69       | 33               | 22           | 37          | 12      | –        | 15                             |
| Modified AspICU                     | –              | –        | –                | –            | –           | –       | –        | –                              |
| Original composite criteria          | 59 (53–69)     | 82       | 66               | 43           | –           | 16      | 10       | 18                             |
| AspICU, modified AspICU, IAPA       | 59 (53–69)     | 82       | 66               | 43           | –           | 16      | 10       | 18                             |
| Modified AspICU                     | 64 (55–76)     | 68       | 47               | 18           | –           | 11      | 7        | –                              |
| Modified AspICU                     | 49 ± 12        | 72       | 26               | 24           | 57          | –       | –        | –                              |
| AspICU                              | –              | –        | –                | –            | –           | –       | –        | –                              |
| Modified AspICU                     | 67 (56–79)     | 60       | –                | –            | –           | –       | –        | –                              |
| EORTC/MSG                           | –              | –        | –                | –            | –           | –       | –        | –                              |
| IAPA                                | –              | –        | –                | –            | –           | –       | –        | –                              |
| AspICU                              | 62 (range, 25–79) | 79     | 31               | 24           | –           | –       | 19       | 5                              |
| ECMM/ISHAM                          | 62 (57–71)     | 73       | –                | 24           | –           | –       | –        | –                              |
| Modified AspICU                     | –              | –        | 31               | 22           | 30          | 5       | –        | –                              |
| EORTC/MSG                           | 65 (range, 44–83) | 72  | –                | 41           | –           | 7       | –        | –                              |
| EORTC/MSG                           | 53 ± 15        | 60       | 37               | 13           | –           | 2       | 4        | 0                              |
| AspICU, IAPA                        | 57 (48–64)     | –        | 26               | 28           | 20          | 6       | –        | –                              |

Patients with CAPA who received systemic steroids

| Patients with CAPA who received tocilizumab | Patients with CAPA who received antifungal therapy |
|--------------------------------------------|-----------------------------------------------|
| 6 (67)                                     | 2 (22)                                        |
| 18 (60)                                    | 22 (73)                                       |
| 16 (53)                                    | 5 (83)                                        |
| 2 (10)                                     | –                                             |
| 9 (47)                                     | 7 (100)                                       |
| 1 (50)                                     | 5 (100)                                       |
| 3 (100)                                    | 3 (100)                                       |

(Continues)
such as systemic steroids and tocilizumab were used with varied frequencies, which may have affected a patient’s susceptibility to aspergillosis.

Mortality from previous reports also varied between 22%\textsuperscript{35} and 100%.\textsuperscript{11} Based on our pooled estimate at 55%, the mortality of patients who develop CAPA may be higher than that of average ICU patients with COVID-19 who received mechanical ventilation observed in a large, international, multicentre, prospective cohort study in Europe (28-day mortality: 31%, 90-day mortality: 37%).\textsuperscript{42} Two observational studies also reported excess mortality rates compared with patients without CAPA.\textsuperscript{7,16} Although it remains unclear whether CAPA directly contributes to death or just unequally affects the most severely ill patients (ie patients with severe ARDS), the presence of CAPA likely represents a higher risk of death. The high heterogeneity in mortality among studies can most likely be explained by the limited number of patients with CAPA and the differences in antifungal treatment strategies. Knowing the mortality with greater certainty based on this meta-analysis may allow us to more accurately prognosticate patients with COVID-19 who develop CAPA in the ICU, which could lead to better goals of care discussions.

Our study has several limitations. First, our meta-analysis included many retrospective observational studies (the ratio of retrospective to prospective studies was approximately 2:1), which could predispose it to reporting bias. Second, the incidence and mortality of CAPA will likely continue to change due to several reasons. Our analysis integrated patients classified as pulmonary aspergillosis by different criteria, as there were no absolute definitions for CAPA. Our pooled estimates were also based on the results mainly from the first wave of the pandemic before the RECOVERY trial was published. With universal administration of systemic steroids to patients with severe COVID-19, overall mortality will likely decrease, but an increase in the incidence of CAPA is possible.\textsuperscript{33,44} The incidence and mortality under the current treatment strategy will likely change based on the new case definitions for CAPA.\textsuperscript{5} Third, 23 out of 28 studies included were reported from Europe, which may potentially limit its applicability in other regions.\textsuperscript{3} Finally, this meta-analysis does not give any insight into whether CAPA contributed to increased mortality compared with critically ill patients with COVID-19 who did not develop CAPA since outcome data for all patients in the ICU were not available.

In conclusion, this meta-analysis provides integrated and refined estimates for the incidence and mortality of CAPA. Our findings can be utilised as a basis for surveillance of CAPA and prognostication in the ICU. Large, prospective cohort studies based on the new case definitions of CAPA are warranted to validate our estimates of incidence and mortality in this important complication of COVID-19.

### TABLE 1 (Continued)

| Author | Patients with COVID-19 in the ICU | Patients with CAPA | Days from COVID-19 diagnosis | Days from ICU admission |
|--------|----------------------------------|--------------------|----------------------------|------------------------|
| Machado et al | 239 | 8 | - | 15 (10-19) |
| Maes et al | 81 | 3 | - | - |
| Nasir et al | 23 | 5 | 8 (2-10) | - |
| Permpalang et al | 396 | 39 | 15 (9-23) | 12 (3-22) |
| Razazi et al | 90 | 7 | - | - |
| Ria et al | 86 | 10 | - | - |
| Roman-Montes et al | 144 | 14 | - | 8.5 (3-13) |
| Rutsaert et al | 34 | 4 | - | - |
| Sarrazy et al | 131 | 4 | - | - |
| Segrelles-Calvo et al | 215 | 7 | - | - |
| van Arkel et al | 31 | 6 | - | 5 (range, 3-28) |
| Van Biesen et al | 53 | 9 | - | 3 (1-4) |
| van Grootveld et al | 63 | 11 | - | 8 (range, 2-23) |
| Vélez Piñado et al | 83 | 16 | 13 (9-20) | 6 (4-9) |
| Versyck et al | 54 | 2 | - | - |
| Wang et al | 26 | 8 | - | - |
| White et al | 257 | 25 | - | - |

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; CAPA, COVID-19-associated Pulmonary Aspergillosis; CKD, Chronic Kidney Disease; COPD, Chronic Obstructive Pulmonary Disease; ECMM/ISHAM, European Confederation for Medical Mycology and International Society for Human and Animal Mycology; EORTC/MSG, European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group; IAPA, Influenza-associated Pulmonary Aspergillosis; ICU, Intensive Care Unit; MV, Mechanically Ventilated; UK, United Kingdom; USA, United States of America.

\textsuperscript{*}All studies were conducted in 2020 and focused on adult patients with COVID-19 unless indicated otherwise. Values are mean ± SD or median (interquartile range) unless indicated otherwise. Dashes indicate that data were not available.
| Days from COVID-19 diagnosis | Days from ICU admission | Patients with CAPA who received systemic steroids | Patients with CAPA who received tocilizumab | Patients with CAPA who received antifungal therapy |
|-----------------------------|------------------------|-----------------------------------------------|----------------------------------------|---------------------------------|
| 8 (100)                    | 8 (100)                | 5 (63)                                        |                                        |                                 |
| 0 (0)                      |                        | 3 (100)                                       |                                        |                                 |
| 4 (80)                     | 3 (60)                 | 5 (100)                                       |                                        |                                 |
| 26 (67)                    | 9 (23)                 | 19 (49)                                       |                                        |                                 |
| -                          | -                      | -                                             |                                        |                                 |
| -                          | -                      | -                                             |                                        |                                 |
| 1 (7)                      | 4 (29)                 | 12 (86)                                       |                                        |                                 |
| -                          | -                      | 4 (100)                                       |                                        |                                 |
| -                          | -                      | 3 (75)                                        |                                        |                                 |
| 4 (57)                     | 5 (71)                 | 4 (57)                                        |                                        |                                 |
| 2 (33)                     |                        | 6 (100)                                       |                                        |                                 |
| 1 (11)                     |                        | 9 (100)                                       |                                        |                                 |
| -                          | -                      | 6 (55)                                        |                                        |                                 |
| 2 (13)                     | 12 (75)                | -                                             |                                        |                                 |
| 2 (100)                    | 1 (50)                 | 2 (100)                                       |                                        |                                 |
| 6 (75)                     |                        | -                                             |                                        |                                 |
| 16 (64)                    |                        | -                                             |                                        | 19 (76)                        |

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; CAPA, COVID-19-associated Pulmonary Aspergillosis; CKD, Chronic Kidney Disease; COPD, Chronic Obstructive Pulmonary Disease; ECMM/ISHAM, European Confederation for Medical Mycology and International Society for Human and Animal Mycology; EORTC/MSG, European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group; IAPA, Influenza-associated Pulmonary Aspergillosis; ICU, Intensive Care Unit; MV, Mechanically Ventilated; UK, United Kingdom; USA, United States of America.

aAll studies were conducted in 2020 and focused on adult patients with COVID-19 unless indicated otherwise. Values are mean ± SD or median (interquartile range) unless indicated otherwise. Dashes indicate that data were not available.

**FIGURE 2** Forrest plot showing the pooled estimate of the incidence of COVID-19-associated pulmonary aspergillosis in the ICU
CONFLICT OF INTEREST
There are no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS
Hayato Mitaka: Conceptualization (lead); Data curation (lead); Formal analysis (equal); Investigation (lead); Methodology (equal); Writing-original draft (lead). Toshiaki Kuno: Data curation (supporting); Formal analysis (equal); Investigation (supporting); Methodology (lead); Supervision (lead); Writing-review & editing (equal). Hisato Takagi: Methodology (supporting); Supervision (supporting); Writing-review & editing (supporting). Paru Patrawalla: Conceptualization (supporting); Investigation (supporting); Project administration (supporting); Supervision (equal); Writing-review & editing (equal).

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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