

Table S2. Observational studies reporting CAPA.

Author/ Country/ Algorithm	Cases/ total (%)	Males (%) / Median age years (IQR)	Underlying diseases (No. of patients)	Days from ICU/TI to CAPA median (IQR)	No. culture-positive samples/total (sample type) <i>Aspergillus</i> spp. (n)	No. of GM- positive samples/total (sample type)/ Median ODI	No. of PCR- positive samples/total (sample type)	No. of BDG positive samples/ total	Specific imaging findings/Type (No. of patients)	Patients treated (%)/Anti-fungal agents (No. of patients)	No. of deaths (%)
Bartoletti [20]/ Italy/ mAspICU	30/108 (27.8)	24 (80)/ 63 (57-70)	Obesity (10), AH (16), DM (5), CVD (6), CPD (4), SOT (1)	4	19/30 (BAL) <i>A. fumigatus</i> (15) <i>A. niger</i> (3) <i>A. flavus</i> (1)	1/30 (serum)/- 30/30 (BAL)/3.5	20/30 (BAL)	-	-	16 (53.3) Voriconazole (13) Other (3)	16 (53.3)
Chen [21]/ China/ NR	1/99 (1%)	-	-	-	1/NR <i>A. flavus</i> (1)	-	-	-	-	-	-
Koehler [22]/ Germany/ AspICU pers.*	5/19 (26.3)	3 (15.7)/ 62 (54-72)	Obesity (1), AH (3), DM (1), CPD (2)	-	1/3 (BAL) 2/3 (TA) <i>A. fumigatus</i> (3)	2/5 (serum)/1.7 3/3 (BAL)/2.5	3/3 (BAL) 1/2 (TA)	-	5/5 Nodules (5) Cavity (1) Air-crescent (1)	5 (100) Voriconazole (4) Isavuconazole (1) Caspofungin (2)	3 (60)
Lahmer [23]/ Germany/ AspICU pers.**	11/32 (34.3)	7 (63.6)/ 72 (58-84)	AH (7), DM (3), CVD (2), CPD (2), CKD(1)	4 (1-7)	9/11 (BAL) <i>A. fumigatus</i> (9)	4/11 (serum)/1.5 11/11 (BAL)/6.4§	-	-	-	11 (100) Voriconazole (5) Isavuconazole (1) Amb (5)	4 (36.3)
Rutsaert [24]/ Belgium/ AspICU	7/34 (20.5)	7 (100)/ 66 (56-77)	Obesity (2), AH (3), DM (3), CVD (1), CKD (1), AML (1), pemphigus (1)	8 (5-13)	5/6 (BAL) 1/1 (TA) <i>A. fumigatus</i> (5) <i>A. flavus</i> (1) Positive DE: 4 (BAL)	1/6 (serum)/0.8 5/6 (BAL)/2.63	-	-	0/7	6 (85.7) Voriconazole (6) Isavuconazole (2)	4 (57.1)
Alanio [11]/ France/ AspICU Pers.***	9/27 (33.3)	5 (71.4)/ 63 (50-76)	Obesity (3), AH (7), DM (3), CVD (2), CPD (1), myeloma (1), steroids (2)	-	5/7 (BAL) 2/2 (BAS) <i>A. fumigatus</i> (7)	1/9 (serum)/0.51 2/7 (BAL)/2.4	3/7 (BAL) 1/2 (TA) 0/8 (serum)	4/7	1/9 Nodules (1)	2 (22.2) Voriconazole (1) Caspofungin (1)	4 (44.4)
Brown [25]/ UK/ IAPA	2/62 (3.2)	2 (100)/ 33.5	AML (1), HSCT (1)	-	1/2 (TA) <i>A. fumigatus</i> (1)	0/2 (serum) 2/2 (TA)	2/2 (TA)	0/2	0/2	2 (100) Posaconazole (1) Itraconazole (1) Caspofungin (1)	1 (50)
Van Arkel [26]/ Netherland/ mAspICU	6/31 (19.4)	6 (100)/ 62 (57-75)	CVD (1), CPD (1), Systemic steroids (3).	5 (3-14)	2/3 (BAL) 2/2 (TA) 1/1 (sputum) <i>A. fumigatus</i> (5)	-	-	-	0/6	6 (100) Voriconazole (5) Anidulafungin (5) AMB (1)	4 (66.7)
Nasir [27]/ Pakistan/ NR	5/147 (3.4)	3 (60)/ 71 (54-83)	AH (3), DM (4)	8 (1-13)	5/5 (TA) <i>A. flavus</i> (3) <i>A. niger</i> (1) <i>A. fumigatus</i> + <i>A.</i> <i>flavus</i> (1)	0/5 (serum)	-	2/5	0/5	5 (100) Voriconazole (3) AMB (2)	3 (60)

Gangneux [10]/ France/ AspICU Pers. °	7/45 (15.6)	4 (57.1) / 70 (63-75)	Obesity (1), AH (3), DM (2), CKD (1), hemopathy (1), CML (1), SOT(1)	-	6/7 (RS) <i>A. fumigatus</i> (6)	2/7 (serum)	7/7 (RS) 3/7 (serum)	-	0/7	7 (100) Voriconazole (4) Isavuconazole (3)	2 (28.6)
Falces-Romero [28]/ Spain/ AspICU- EORTC	8/5700 (0.1)	6 (75)/ 69 (61-72)	Obesity (2), DM (5), CPD (2), HIV (1), MDS (1), Haemophilia (1), AS (1), Golimumab (1)	12 (7-21)	8/8 (BAS) 1/1 (BAL) 1/1 (sputum) <i>A. fumigatus</i> (9) <i>A. nidulans</i> (1)	1/2 (serum)/1.97 2/2 (BAL)/3	-	-	0/10	8 (100) Voriconazole (5) Isavuconazole (2) Caspofungin (1) Anidulafungin (1) AMB (5)	7 (87.5)
Zhang [29]/ China/ NR	3/38 (7.9)	-	-	-	3/NR (RS) 2 <i>Aspergillus</i> spp. <i>A. fumigatus</i>	-	-	-	-	-	-
White [30]/ UK/ CAPA	25/135 (18.5)	-	Obesity (6), AH (8), DM (6), CVD (1), CPD (12), CKD (2), cancer (6)	8 (0-35)	12/12 (BAL) <i>A. fumigatus</i> (11) <i>A. versicolor</i> (1)	2/4 (serum)/2.9 17/19 (BAL)/5.6	14(14 (BAL) 5/5 (Serum)	13/14	12/25 Nodules (7) Cavity (5) Fungus ball (1)	18 (72) Voriconazole (14) Fluconazole (2) Caspofungin (2) Anidulafungin (2) AMB (5)	13 (52)
Ichai [31]/ France/ NR	6/26 (23.1)	-/ 64 (mean)	-	6.5 (mean)	-	-	-	-	-	6 (100) Voriconazole (1) Isavuconazole (5)	2 (33.3)
Sarrazyn [32]/ Belgium/ AspICU	4/131 (3.1)	3 (75)/ 75 (69-89)	Obesity (2), CKD (1)	4	4/4 (BAL) <i>Aspergillus</i> spp. (4)	4/4 (BAL)	2/4 (BAL)	-	0/4	3 (75) Voriconazole (2) AMB (1)	4 (100)
Dupont [33]/ France/ AspICU Pers. °°	19/106 (17.9)	15 (79)/ 69 (62-73)	Obesity (1), AH (7), DM (7), CVD (1), CPD (8), cancer (4), CKD (2), HIV (1), HBV (1)	10 (7-15)	7/8 (BAL) 6/6 (BAS) 3/4 (TA) <i>A. fumigatus</i> (14) <i>A. niger</i> (1) <i>A. calidoustus</i> (1) Positive DE: 2 (BAL) + 1 (TA)	5/9 (BAL)/1.57	-	-	3/19 Nodules (2) Cavity (2)	9 (47.3) Voriconazole (9) Caspofungin (1)	7 (36.8)
Mitaka [34]/ USA/ AspICU	4/7 (57.1)	4 (100)/ 78 (77-80)	AH (1), DM (1), CVD (2),CPD (1), cancer (2)	10 (8-12)	4/4 (BAL) <i>A. fumigatus</i> (4)	1/4 (serum)	-	-	1/4 Cavity (1) Air-crescent (1)	4 (100) Voriconazole (3) Caspofungin (1)	4 (100)
Borman [35]/ UK/ AspICU Pers. °°°	15/61 (24.6)	9 (60)/ 57 (48-66)	-	-	2/4 (BAL) 2/3 (TA) 1/1 (sputum) <i>A. fumigatus</i> (5) Positive DE: 1 (BAL)	5/15 (serum)/1.7 4/5 (BAL)/5.2	2/3 (BAL) 1/8 (serum)	12/15	-	-	-

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Fekkar [45]/ France/ EORTC	6/260 (2.3)	5 (83.3)/ 56 (49-72)	Obesity (5), AH (5), DM (1), SOT (3)	10 (6-42)	3/4 (BAL) 2/2 (TA) <i>A. fumigatus</i> (3)	1/6 (serum)/1.19 2/5 (BAL)/1.5	2/2 (TA) 2/2 (BAL) 2/6 (Serum)	2/6	-	5 (83.3) Voriconazole (5) Isavuconazole (5) Caspofungin (5) AMB 82)	4 (66.7)
Gouzien [46]/ France/ mAspICU	2/53 (3.8)	-	-	-	2/53 <i>Aspergillus</i> spp. (1 BAL, 1 TA)	1/53 (serum)	-	-	-	1	-
Van Grootveld [47]/ Netherlands/ ECMM	11/63 (17.5)	14 (73.7)/ 65 (59-72)	AH (6), DM (5), CVD (3), CPD (7), PT (2), cancer (1)	17 (14-21)&	3/11 (BAL) 4/8 (TA) <i>A. fumigatus</i> (7)	10/11 (BAL)/4.4	6/11 (BAL) 7/8 (BAS)	-	-	9 (47.4) AMB (9) Voriconazole (5)	10 (52.6)
Positive DE: 1 (BAL)											
Maes [48]/ UK/ IAPA	3/94 (3.2)	-	-	-	0/3 (BAL)	3/3 (BAL)/1	1/3 (BAL)	-	-	3 (100) AMB (3)	2 (66.7)
Meijer [49]/ Netherlands/ ECMM	13/66 (19.7)	10 (76.9)/ 68 (62-74)	AH (2), DM (3), CVD (7), CPD (1), UC (2), CKD (1)	-	8/8 (BAL) 5/5 (TA) <i>A. fumigatus</i> (13)	0/6 (serum) 4/5 (TA) + 2/12 (BAL)/4.5	4/5 (BAL) 2/2 (TA)	1/1	2/13 Nodules (1) Cavity (1)	13 (100) Voriconazole (13) Caspofungin (5) AMB (5)	6 (46.1)
Van Biesen [50]/ Netherlands/ Personal \$\$\$	9/42 (21.4)	6 (66.7)/ 73 (65-75)	Obesity (8), AH (3), DM (1), CPD (4), SOT (1), chronic steroid (1)	3 (1-5)	7/9 (BAL) <i>A. fumigatus</i> (5) <i>A. flavus</i> (1) <i>A. terreus</i> (1)	9/9 (BAL)/4	-	-	0/9	9 (100) Voriconazole (9) AMB (9)	2 (22.2)
Obata [51]/ USA/ NR	4/226 (1.8)	-	-	-	-	-	-	-	-	-	-
Razazi [52]/ France/ mAspICU- IAPA	7/90 (7.8)	-	-	6 (5-11)	4/24 (BAL) <i>Aspergillus</i> spp. (4)	5/88 (serum)	-	9/88	-	-	-
Positive DE: 2 (BAL)											
Ripa [2]/ Italy/AspICU Pers. ^^^	11/731 (1.5)	-	-	-	8/NR (4 BAL, 4 BAS) <i>A. fumigatus</i> (7) <i>A. terreus</i> (1)	6/NR (BAL)	-	-	-	-	-
Pintado [53]/ Mexico/ ECMM	16/83 (19.3)	11 (68.8)/ 64 (mean)	Obesity (6), AH (4), DM (5), CPD (1), cancer (3)	6 (4-9)	2/16 (BAL) <i>A. fumigatus</i> (2)	7/16 (serum) 9/16 (BAL)	-	-	-	-	5 (31.3)
Versych [54]/ France/ IAPA	2/54 (3.7)	2 (100)/ 63.5	AH (1), DM (1)	6.5	1/1 (BAL) 1/1 (TA) <i>A. fumigatus</i> (2)	2/2 (serum)/2.34 1/2 (BAL)/2.46	-	2/2	2/2 Cavity (2) Nodules (1) Halo sign (1)	2 (100) Voriconazole (2)	2 (100)
Negative DE: 1 (BAL)											

Reizine [55]/ France/ ECMM	10/49 (20.4)	6 (60)/ 72 (57-77)	Obesity (1), DM (2), CKD (1), CML (1), SOT (1)	6 (3-12)	8/10 (BAS) 1/10 (sputum) <i>A. fumigatus</i> (9)	3/10 (serum) 4/10 (BAS)	9/10 (BAS)	-	Wedge-cons. (7) Halo sign (1)	8 (80) Voriconazole (6) Isavuconazole (4)	4 (40)
Oliva [56]/ Italy/ mAspICU- IAPA	2/55 (3.6)	2 (100)/ 48.5	Obesity (1)	-	0/2 (RS)	2/2 (RS)/2.3	-	-	0/2	-	0
Campochiaro [57]/Italy/ NR	1/65 (1.5)	1 (100)/ 68	-	-	1/1 (BAL) <i>A. terreus</i> (1)	-	-	-	-	1 (100) Voriconazole (1)	1 (100)
Wasylyshyn [58]/ USA/ECMM	3/256 (1.2)	2 (66.7)/ 67	Obesity (2), AH (2), DM (1), epilepsy (1)	13 §§	2/3 (TA) <i>A. fumigatus</i> (2)	1/2 (serum)/3.1 1/1 (BAL)/1.4	-	-	2/3 Cavity (2)	2 (66.7) Voriconazole (2) Isavuconazole (1) Micafungin (1) AMB (1)	1 (33.3)
Nebreda- Mayoral [59]/ Spain/ NR	3/712 (0.4)	-	-	-	3/3 (BAS) <i>A. fumigatus</i> (2) <i>A. niger</i> (1)	-	-	-	-	3 (100) Voriconazole (2) Isavuconazole (2)	2 (66.7)
Signorini [60]/ Italy/ EORTC	2/92 (2.2)	-	-	-	2/NR <i>Aspergillus</i> spp. (2)	-	-	-	-	-	-
Rabagliati [61]/ Chile/ ECMM	14/146 (9.6)	8 (57.1)/ 65 (55-73)	Obesity (3), AH (7), DM (2), CPD (4)	15 (10-23)	7/14 (TA) <i>A. niger</i> (4) <i>A. fumigatus</i> (3) <i>A. terreus</i> (1) <i>A. lentulus</i> (1)	6/14 (serum)/1.2 2/14 (BAL)/4.6	-	-	1/13 Cavity (1)	11 (78.6) Voriconazole (10) AMB (1)	4 (28.6)
Lamoth [62]/ Switzerland/ mAspICU pers. \$\$	3/118 (2.5)	3 (100)/ 62 (mean)	Obesity (2), A H (2), DM (1), CPD (1)	7 (3-8)	3/3 (TA) <i>A. fumigatus</i> (3)	1/3 (serum)/0.73	1/3 (TA)	1/3	0/3	3 (100) Voriconazole (3)	1 (33.3)
Yang [63]/ China/ NR	2/52 (3.8)	-	-	-	2/NR (RS) <i>A. fumigatus</i> (1) <i>A. flavus</i> (1)	-	-	-	-	-	-

Data are absolute number (percentage) unless otherwise specified.

Abbreviations. DE, direct examination of respiratory sample showing septate branching hyphae; AH, arterial hypertension; DM, diabetes mellitus; CVD, cardiovascular disease; CPD, chronic pulmonary disease; SOT, solid organ transplant; ICU, intensive care unit; IQR, interquartile range; TI, tracheal intubation; ODI, optical density index; BDG, (1,3)-beta-D-glucan; BAL, bronchial alveolar lavage; TA, tracheal aspirate; BAS, bronchial aspirate; CKD, chronic kidney disease; AML, acute myeloid leukaemia; HSCT, haematopoietic stem cell transplantation; CML, chronic myeloid leukaemia; HIV; human immunodeficiency virus; MDS, myelodysplastic syndrome; AS, ankylosing spondylitis; CLL, chronic lymphocytic leukaemia; PT, pulmonary thromboembolism; UC, ulcerative colitis; RS, respiratory specimen, AMB, amphotericin B.

* Modified AspICU algorithm with the addition that positive galactomannan GM (≥ 1) from BAL or TA, or two consecutively but separately drawn positive serum samples (≥ 1) were accepted as entry criterion.

** Putative IPA was assumed in one of the following conditions: cultural growth of *Aspergillus* spp from BAL specimens.; GM optical density index (ODI) >0.5 in serum, GM ODI >1 in respiratory tract specimen from BAL. Clinical signs and radiological signs were in line with the modified AspICU score and CAPA definitions.

*** Putative IPA was considered if *Aspergillus* spp were identified in BAL culture; or if two of the following conditions were met (ie, presence of *Aspergillus* spp in bronchial aspiration (BAS) culture; positive *Aspergillus fumigatus* qPCR in BAL, BA, or serum; galactomannan ODI >0.8 in BAL; GM ODI >0.5 in serum; and β -D-glucan >80 pg/mL in serum).

° putative IA: AspICU algorithm which includes PCR together with culture; probable IA: putative IA + one positive blood biomarker (GM and/or PCR).

°° AspICU algorithm plus BAL GM results; COVID-19 considered as a risk factor.

°°° modified AspICU algorithm incorporating PCR, serology, and angioinvasion biomarkers as proposed by Gangneux.

^ modified AspICU algorithm by Schauwvlieghe, considering a positive serum GM or *Aspergillus* spp. growth from a TA, since bronchoscopies were not performed at Authors' institution due to safety concerns for healthcare workers.

^^ Probable CAPA: presence of new cavitary lung lesion(s) on chest CT without alternative explanation, positive serum GM EIA index ≥ 0.5 , positive BAL GM index ≥ 1.0 , or positive culture for *Aspergillus* species in BAL. Possible CAPA: positive BAL GM index 0.5 – 1.0; positive serum BDG ≥ 80 pg/ml without alternative explanation; or culture with growth of *Aspergillus* species in TA.

^^^ AspICU algorithm plus serum or BAL GM index.

\$ AspICU by Blot, IAPA by Schauwvlieghe and EORTC algorithm.

\$\$ mAspICU by Verweij. Results of BAS cultures were also considered for defining a putative IPA category (*Aspergillus* spp. recovered from culture of ≥ 2 consecutive BAS in the absence of bronchoscopy and BAL sample).

\$\$\$ AspICU algorithm without the host risk factor+ BAL GM index.

§ In CAPA non-survivors; median was 4.6 days in CAPA-survivors.

§§ Median days since COVID-diagnosis to CAPA.

& Median days since symptoms onset to CAPA.