



Figure 1. legend. VAP, ventilator-associated pneumonia.

Table S1. List of participating centres.

Center	No. of participating ICU (number of beds)
Ospedale Policlinico San Martino – IRCCS, Genoa*	2 (39)
Azienda Sanitaria Universitaria Giuliano-Isontina (ASUGI), Trieste	1 (16)
Cotugno Hospital, AORN dei Colli, Naples, Italy	2 (24)
Policlinico S. Orsola Hospital, Bologna, Italy	1 (60)
Maggiore Hospital, Bologna, Italy	1 (10)
Bellaria Hospital, Bologna, Italy	1 (26)
Azienda Ospedaliera Universitaria Pisana. Pisa, Italy	1 (50)
Policlinic Hospital, Modena	1 (33)
Città della Salute e della Scienza Hospital, Turin, Italy	1 (24)

* coordinating center.

Table S2. Isolates from BALF cultures.

Isolate/s	No. of patients 77 (100)
<i>Pseudomonas aeruginosa</i>	19 (25)
<i>Staphylococcus aureus</i>	13 (17)
<i>Klebsiella pneumoniae</i>	9 (12)
<i>Acinetobacter</i> spp.	6 (8)
<i>Enterobacter aerogenes</i>	4 (5)
<i>Serratia marcescens</i>	3 (4)
<i>Klebsiella oxytoca</i>	2 (3)
<i>Acinetobacter</i> spp. plus <i>Klebsiella pneumoniae</i>	2 (3)
<i>Staphylococcus aureus</i> plus <i>Stenotrophomonas maltophilia</i>	2 (3)
<i>Staphylococcus aureus</i> plus <i>Klebsiella pneumoniae</i>	2 (3)
<i>Pseudomonas aeruginosa</i> plus <i>Stenotrophomonas maltophilia</i>	2 (3)
<i>Citrobacter</i> spp.	1 (1)
<i>Chryseobacterium indologenes</i>	1 (1)
<i>Escherichia coli</i>	1 (1)
<i>Haemophilus influenzae</i>	1 (1)
<i>Morganella morganii</i>	1 (1)
<i>Pseudomonas aeruginosa</i> plus <i>Escherichia coli</i>	1 (1)
<i>Pseudomonas aeruginosa</i> plus <i>Klebsiella pneumoniae</i>	1 (1)
<i>Pseudomonas aeruginosa</i> plus <i>Proteus</i> spp.	1 (1)
<i>Pseudomonas aeruginosa</i> plus <i>Serratia marcescens</i>	1 (1)
<i>Staphylococcus aureus</i> plus <i>Enterobacter aerogenes</i>	1 (1)
<i>Pseudomonas aeruginosa</i> plus <i>Acinetobacter</i> spp. plus <i>Enterobacter aerogenes</i>	1 (1)
<i>Pseudomonas aeruginosa</i> plus <i>Klebsiella pneumoniae</i> plus <i>Proteus</i> spp.	1 (1)
<i>Stenotrophomonas maltophilia</i> plus <i>Enterobacter aerogenes</i> plus <i>Proteus</i> spp.	1 (1)

Table S3. Descriptive comparison of the demographic and clinical characteristics of patients with and without BALF culture.

Variable	BALF culture available* 79 (46)	No BALF culture available 92 (54)	<i>p</i> **
Demographics			
Age in years, median (IQR)	62 (57-69)	66 (57-72)	0.259
Male gender	62 (78)	75 (82)	0.619
BMI in kg/m ² , median (IQR)	27 (24-30)	28 (26-30)	0.357
Baseline comorbidities			
Diabetes mellitus	18 (23)	21 (23)	0.095
Hypertension	55 (70)	54 (59)	0.138
Smoking/respiratory disease	11 (14)	15 (16)	0.666
End-stage renal disease	4 (5)	6 (7)	0.754
Moderate/severe liver failure	3 (4)	0 (0)	0.097
Neurologic disease	6 (8)	0 (0)	0.009
Solid cancer	2 (3)	9 (10)	0.054
Hematological malignancy*	1 (1)	3 (3)	0.625
HIV infection	0 (0)	0 (0)	-
Previous antibiotic therapy			
Any*	75 (95)	87 (95)	1.000
Semisynthetic penicillins	33 (42)	43 (47)	0.515
Cephalosporins	44 (56)	44 (48)	0.305
Carbapenems	10 (13)	15 (16)	0.501
Polymyxins	0 (0)	2 (2)	0.500
Glycopeptides	3 (4)	7 (8)	0.344
Oxazolidinones	13 (17)	25 (27)	0.093
Macrolides	27 (34)	51 (55)	0.005
Fluoroquinolones	3 (4)	2 (2)	0.663
Aminoglycosides	0 (0)	0 (0)	-
Previous anti-inflammatory therapy			
Steroids	57 (72)	51 (55)	0.024
NSAIDs	34 (43)	6 (7)	<0.001
Chloroquine/Hydroxychloroquine	75 (95)	84 (91)	0.354
Anti-IL-6 receptor monoclonal antibodies	45 (57)	64 (70)	0.087
Monoclonal IL-1 receptor antagonists	3 (4)	2 (2)	0.663
VAP characteristics			
Days of invasive ventilation before VAP, median (IQR)	10 (4-17)	9 (5-13)	0.821
SOFA score at VAP onset, median (IQR)	7 (5-9)	6 (3-9)	0.079

Tracheostomy before VAP	30 (38)	19 (21)	0.013
Presence of septic shock at VAP onset	47 (60)	33 (36)	0.002
Presence of ARDS at VAP onset	53 (67)	79 (86)	0.004
Presence of AKI at VAP onset	25 (32)	16 (17)	0.030
Need for hemodialytic therapy at VAP onset	9 (11)	8 (9)	0.557
Need for ECMO at VAP onset*	5 (6)	8 (9)	0.560
Presence of coagulative disorders at VAP onset			0.094
None	57 (72)	75 (82)	
Thrombotic	10 (13)	10 (11)	
Hemorrhagic	12 (15)	5 (5)	
Both	0 (0)	2 (2)	
BSI at VAP onset	45 (57)	31 (34)	0.002
VAP treatment			
Antibiotic treatment within 24 h of VAP onset	66 (84)	59 (64)	0.004
IgM-enriched intravenous immunoglobulins	5 (6)	5 (5)	1.000
Cytokine blood filtration	16 (20)	2 (2)	<0.001
Outcome			
30-day case fatality	33 (42)	45 (49)	0.350

Results are reported as number of patients (%) unless otherwise indicated. AKI, acute kidney injury; ARDS; acute respiratory distress syndrome; BALF, bronchoalveolar lavage fluid; BMI, body mass index; BSI, bloodstream infection; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; HIV, human immunodeficiency virus; ICU, intensive care unit; IQR, interquartile range; NSAIDs, nonsteroidal anti-inflammatory drugs; SOFA, sequential organ failure assessment; VAP, ventilator-associated pneumonia. * Only 2/79 (2.5%) patients had negative BALF culture, whereas 77/79 (97.5%) had positive BALF culture results. ** Descriptive comparison by means of chi-square or Fisher exact tests for categorical variables, as appropriate, and Mann-Whitney U test for continuous variables.

Table S4. Univariable analysis of factors associated with 30-day case fatality in critically ill COVID-19 patients with BALF-positive VAP.

Variable	Non-survivors 32 (42)	Survivors 45 (58)	OR (95% CI)	<i>p</i>
Demographics				
Age in years, median (IQR)	63 (58-72)	63 (57-69)	1.01 (0.97-1.06)	0.592
Male gender	23 (72)	36 (80)	0.64 (0.22-1.85)	0.408
BMI in kg/m ² , median (IQR)	26 (24-33)	28 (25-30)	1.00 (0.99-1.02)	0.756
Baseline comorbidities				
Diabetes mellitus	9 (28)	8 (18)	1.81 (0.61-5.36)	0.284
Hypertension	24 (75)	30 (67)	1.50 (0.55-4.13)	0.432
Smoking/respiratory disease	9 (28)	12 (27)	1.08 (0.39-2.97)	0.887
End-stage renal disease	2 (6)	1 (2)	2.93 (0.25-33.82)	0.388
Moderate/severe liver failure	2 (6)	1 (2)	2.93 (0.25-33.82)	0.388
Neurologic disease	1 (3)	4 (9)	0.33 (0.04-3.11)	0.333
Solid cancer	1 (3)	1 (2)	1.42 (0.09-23.57)	0.807
Hematological malignancy*	1 (3)	0 (0)	4.33 (0.22-640.80)	0.333
HIV infection	0 (0)	0 (0)	-	-
Previous antibiotic therapy				
Any*	28 (88)	45 (100)	0.07 (0.00-0.69)	0.019
Semisynthetic penicillins	15 (47)	19 (42)	1.21 (0.49-3.01)	0.685
Cephalosporins	13 (41)	29 (64)	0.38 (0.15-0.96)	0.041
Carbapenems	3 (9)	4 (9)	1.06 (0.22-5.10)	0.942
Polymyxins	0 (0)	0 (0)	-	-
Glycopeptides	1 (3)	1 (2)	1.42 (0.09-23.57)	0.807
Oxazolidinones	7 (22)	5 (11)	2.24 (0.64-7.83)	0.207
Macrolides	11 (34)	17 (38)	0.86 (0.34-2.22)	0.760
Fluoroquinolones	2 (6)	1 (2)	2.93 (0.25-33.82)	0.388
Aminoglycosides	0 (0)	0 (0)	-	-
Previous anti-inflammatory therapy				
Steroids	21 (66)	34 (76)	0.62 (0.23-1.67)	0.344
NSAIDs	9 (28)	24 (53)	0.34 (0.13-0.90)	0.030
Chloroquine/Hydroxychloroquine	30 (94)	43 (96)	0.70 (0.09-5.23)	0.726

Anti-IL-6 receptor monoclonal antibodies	15 (47)	30 (67)	0.44 (0.17-1.12)	0.085
Monoclonal IL-1 receptor antagonists	2 (6)	1 (2)	2.93 (0.25-33.82)	0.388
VAP characteristics				
Days of invasive ventilation before VAP, median (IQR)	9 (4-18)	12 (5-17)	0.99 (0.93-1.04)	0.617
SOFA score at VAP onset, median (IQR)	7 (5-11)	7 (5-8)	1.14 (0.98-1.33)	0.082
Tracheostomy before VAP	7 (22)	21 (47)	0.32 (0.12-0.89)	0.029
Presence of septic shock at VAP onset	25 (78)	21 (47)	4.08 (1.47-11.35)	0.007
Presence of ARDS at VAP onset	31 (97)	21 (47)	35.43 (4.45-282.36)	0.001
Presence of AKI at VAP onset	13 (41)	11 (24)	2.12 (0.79-5.63)	0.134
Need for hemodialytic therapy at VAP onset	5 (16)	3 (7)	2.59 (0.57-11.75)	0.217
Need for ECMO at VAP onset*	4 (13)	0 (0)	14.37 (1.45-1931.17)	0.019
Presence of coagulative disorders at VAP onset				0.426
None	22 (69)	34 (76)	Ref.	
Thrombotic	3 (9)	6 (13)	0.73 (0.18-3.42)	
Hemorrhagic	7 (22)	5 (11)	2.16 (0.61-7.68)	
Both	0 (0)	0 (0)	-	
Microorganisms isolated from BALF				0.514
<i>Pseudomonas aeruginosa</i>	9 (28)	18 (40)	0.64 (0.22-1.86)	
<i>Staphylococcus aureus</i>	9 (28)	9 (20)	1.29 (0.40-4.09)	
Other than <i>P. aeruginosa</i> and <i>S. aureus</i>	14 (44)	18 (40)	Ref.	
Isolation of resistant organisms from BALF				0.876
MRSA	4 (13)	4 (9)	1.44 (0.32-6.54)	
Carbapenem-resistant Gram-negative bacteria	10 (31)	15 (33)	0.96 (0.35-2.62)	
None of them	18 (56)	26 (58)	Ref.	
BSI at VAP onset	17 (53)	26 (58)	0.83 (0.33-2.06)	0.685

VAP treatment				
Antibiotic treatment within 24 h of VAP onset	26 (81)	38 (84)	0.80 (0.24-2.65)	0.713
Appropriate antibiotic treatment within 24 h of VAP onset	19 (59)	26 (58)	1.07 (0.43-2.68)	0.889
IgM-enriched intravenous immunoglobulins	3 (9)	2 (4)	2.22 (0.35-14.15)	0.397
Cytokine blood filtration	6 (19)	9 (20)	0.92 (0.29-2.91)	0.891

Results are reported as number of patients (%) unless otherwise indicated. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; BALF, bronchoalveolar lavage fluid; BMI, body mass index; BSI, bloodstream infection; CI, confidence intervals; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; HIV, human immunodeficiency virus; ICU, intensive care unit; IQR, interquartile range; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio; SOFA, sequential organ failure assessment; VAP, ventilator-associated pneumonia. * Standard logistic regression model not converging. Results for these variables are from univariable logistic regression models with Firth's correction.

Table S5. Multivariable analysis of independent predictors of 30-day case fatality in critically ill COVID-19 patients with BALF-positive VAP*.

Variable	OR (95% CI)	<i>p</i>
Any previous antibiotic therapy	0.51 (0.00-8.20)	0.673
Previous cephalosporins	0.38 (0.09-1.44)	0.155
Previous NSAIDs	1.59 (0.39-7.19)	0.519
Previous anti-IL-6 receptor monoclonal antibodies	0.52 (0.12-1.95)	0.332
Tracheostomy before VAP	0.30 (0.06-1.15)	0.080
SOFA score at VAP onset	0.94 (0.74-1.19)	0.597
Presence of septic shock at VAP onset	3.69 (0.95-17.49)	0.060
Presence of ARDS at VAP onset	44.09 (5.97-694.29)	<0.001**
Need for ECMO at VAP onset	18.1 (0.81-3366.72)	0.070
Antibiotic treatment within 24 h of VAP onset	0.79 (0.08-7.56)	0.832
Appropriate antibiotic treatment within 24 h of VAP onset	0.38 (0.07-1.74)	0.214

ARDS; acute respiratory distress syndrome; CI, confidence intervals; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio; SOFA, sequential organ failure assessment; VAP, ventilator-associated pneumonia. * Standard logistic regression model not converging. Results are from multivariable logistic regression with Firth's correction. ** $p < 0.05$.