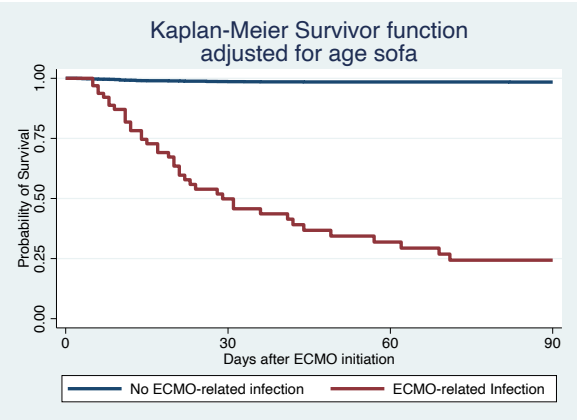


**Figure S1** Adjusted Kaplan-Meier curves of cumulative probabilities of 90-day survival for patients supported by ECMO with or without concomitant ECMO-related infection. ECMO, extracorporeal membrane oxygenation.

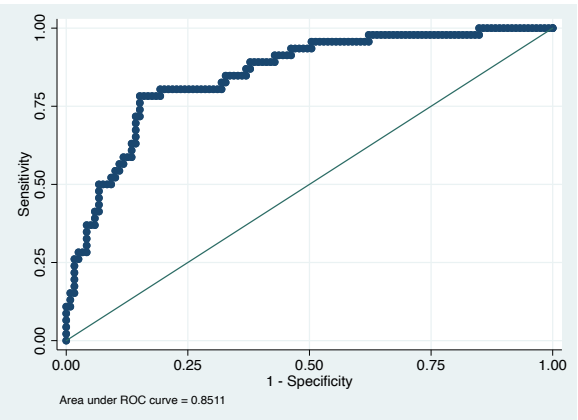


**Figure S2** Receiver operating characteristic curve calculated for multivariate logistic regression of ECMO-related infection. ROC, receiver operating characteristic; ECMO, extracorporeal membrane oxygenation.

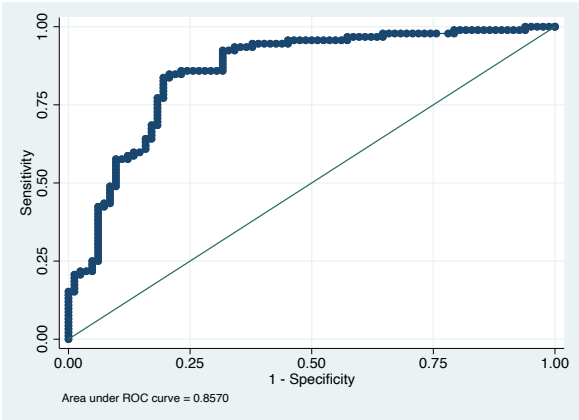


**Figure S3** Receiver operating characteristic curve calculated for multivariate logistic regression of 90-day mortality. ROC, receiver operating characteristic.


https://dx.doi.org/10.21037/jtd-23-1912

**Table S1** Diagnostic criteria for infections during ECMO

| Infection | Clinical features | Site of culture | Bacterial load | Also |
|---|---|---|---|---|
| Ventilator-associated pneumonia[†] | Two following signs:<br>(I) The new onset of fever and purulent sputum<br>(II) Leukocytosis/leucopenia | Bronchoalveolar lavage | $\geq 10^4$ CFU/mL | New or progressive radiographic infiltrate |
| | (III) Declined oxygenation | Endotracheal aspirate | $\geq 10^5$ CFU/mL | |
| Urinary tract infection[‡] | Fever or tachycardia or hypotension | Catheter urine specimen or midstream urine specimen within the previous 48 hours of removing urethral, suprapubic, or condom catheter | $\geq 10^3$ CFU/mL | – |
| Blood stream infection | Fever or tachycardia or hypotension + no further sign of localized infection | At least one blood culture<br>For common skin contaminants (coagulase-negative *Staphylococci, Corynebacterium* species, *Bacillus* species, *Propionibacterium* species, *Aerococcus* species, *Micrococcus* species), two blood cultures with the same antimicrobial susceptibility profile were mandatory or strong clinical grounds that it is not a contaminant | – | – |
| Septic shock | (I) The new onset of hypotension and lactate more than 4 mmol/L<br>(II) Need resuscitation or increased vasoactive agents | – | – | Followed by infection during ECMO |

[†], 48–72 hours after endotracheal intubation or less than 48 hours after extubation; [‡], at least 48 hours after catheterization. ECMO, extracorporeal membrane oxygenation; CFU, colony forming units.

**Table S2** Infection onset times

| Variables | VAP (n=24) | UTI (n=1) | BSI (n=21) |
|---|---|---|---|
| Days from hospital admission | 6.3 [4.3, 9.1] | 10.5 | 9.6 [4.9, 14.5] |
| Days from intubation | 8.0 [5.6, 11.6] | 12.0 | 9.8 [6.9, 14.2] |
| Days from ECMO initiation | 6.2 [4.4, 8.0] | 11.0 | 8.9 [4.8, 11.6] |

Data are presented as median [interquartile range]. VAP, ventilator-associated pneumonia; UTI, urinary tract infection; BSI, blood stream infection; ECMO, extracorporeal membrane oxygenation.


https://dx.doi.org/10.21037/jtd-23-1912

**Table S3** Microorganisms associated with various ECMO-related infections

| Organism | N (%) |
|---|---|
| VAP (n=24) | |
| Gram-negative bacteria | |
| *Acinetobacter baumannii* | 10 (41.7) |
| *Klebsiella pneumoniae* | 5 (20.8) |
| *Pseudomonas aeruginosa* | 2 (8.3) |
| *Stenotrophomonas maltophilia* | 1 (4.2) |
| *Burkholderia cepacia* | 1 (4.2) |
| *Serratia marcescens* | 1 (4.2) |
| Gram-positive bacteria | |
| *Enterococcus* spp. | 1 (4.2) |
| *Staphylococcus aureus* | 1 (4.2) |
| Fungus | |
| *Candida* sp. | 2 (8.3) |
| UTI (n=1) | |
| Fungus | |
| *Candida tropicalis* | 1 (100.0) |
| BSI (n=21) | |
| Gram-negative bacteria | |
| *Acinetobacter baumannii* | 7 (33.3) |
| *Klebsiella pneumoniae* | 5 (23.8) |
| *Burkholderia cepacia* | 2 (9.5) |
| Gram-positive bacteria | |
| *Enterococcus* spp. | 3 (14.3) |
| *Staphylococcus aureus* | 1 (4.8) |
| Fungus | |
| *Candida albicans* | 1 (4.8) |
| *Candida glabrata* | 1 (4.8) |
| *Trichosporon asahii* | 1 (4.8) |
| MDR (n=19) | |
| Gram-negative bacteria | |
| *Acinetobacter baumannii* | 12 (63.2) |
| *Klebsiella pneumoniae* | 6 (31.6) |
| *Burkholderia cepacia* | 1 (5.3) |
| Fungus | NA |

ECMO, extracorporeal membrane oxygenation; VAP, ventilator-associated pneumonia; UTI, urinary tract infection; BSI, blood stream infection; MDR, multi-drug resistant; NA, not available.


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**Table S4** Laboratory characteristics in patients with and without ECMO-related infection

| Variables | Infected patients (n=46) | Uninfected patients (n=128) | P value |
|---|---|---|---|
| Immune status | | | |
| Lymphocyte on day 1 ($10^9$/L) | 0.60 [0.36, 0.87] | 0.92 [0.49, 1.42] | 0.005 |
| Lymphocyte on day 2 ($10^9$/L) | 0.52 [0.36, 1.09] | 0.86 [0.60, 1.41] | <0.001 |
| Lymphocyte on day 3 ($10^9$/L) | 0.52 [0.37, 0.72] | 0.89 [0.55, 1.24] | <0.001 |
| HLA-DR$^+$/CD14$^+$ on day 1 (%)$^\dagger$ | 57.7 [41.5, 92.0] | 73.6 [43.5, 92.4] | 0.485 |
| ΔLym ($10^9$/L) | −0.13 [−0.46, 0.09] | −0.02 [−0.49, 0.39] | 0.036 |
| Inflammation response | | | |
| White blood cell on day 1 ($10^9$/L) | 10.56 [6.10, 14.64] | 13.70 [7.34, 18.75] | 0.048 |
| White blood cell on day 2 ($10^9$/L) | 10.32 [7.07, 15.09] | 12.26 [8.02, 16.31] | 0.262 |
| White blood cell on day 3 ($10^9$/L) | 9.52 [7.88, 14.84] | 11.72 [7.75, 15.83] | 0.265 |
| ΔWBC ($10^9$/L) | 0.29 [−2.89, 3.21] | −1.32 [−4.74, 1.97] | 0.136 |
| Coagulation | | | |
| Platelet on day 1 ($10^9$/L) | 111 [73, 187] | 144 [104, 204] | 0.038 |
| Platelet on day 2 ($10^9$/L) | 100 [65, 169] | 121 [75, 164] | 0.491 |
| Platelet on day 3 ($10^9$/L) | 101 [59, 134] | 103 [71, 139] | 0.735 |
| ΔPlt ($10^9$/L) | −18 [−50, 9] | −31 [−89, 0] | 0.434 |
| D-dimer on day 1 (μg/L) | 2,904 [1,196, 5,946] | 2,234 [699, 5,402] | 0.298 |
| D-dimer on day 2 (μg/L) | 2,905 [1,212, 4,893] | 2,440 [879, 5,070] | 0.404 |
| D-dimer on day 3 (μg/L) | 2,248 [1,090, 4,273] | 2,202 [961, 3,665] | 0.796 |
| ΔD-dimer (μg/L) | −76 [−2,065, 2,129] | 123 [−2,194, 1,859] | 0.863 |

Data are presented as median [interquartile range]. $^\dagger$, missing value 33.3%. ECMO, extracorporeal membrane oxygenation; ΔLym, difference of lymphocyte count between day 3 and day 1; ΔWBC, difference of white blood cell count between day 3 and day 1; ΔPlt, difference of platelet count between day 3 and day 1; ΔD-dimer, difference of D-dimer between day 3 and day 1.


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**Table S5** Blood test and coagulation variable between infected patients and non-infected patients

| Variables | Infected patients, (n=46) | Uninfected patients, (n=128) | P value |
|---|---|---|---|
| Hemoglobin | | | |
| Day 1 | 99 [90, 123] | 122 [102, 135] | 0.005 |
| Day 2 | 104 [89, 120] | 109 [92, 121] | 0.696 |
| Day 3 | 101 [92, 112] | 100 [89, 111] | 0.755 |
| ΔHB | −4 [−16, 10] | −18 [−33, −4] | 0.004 |
| Hematocrit | | | |
| Day 1 | 30.1 [26.8, 37.1] | 35.8 [30.5, 40.0] | 0.003 |
| Day 2 | 31.3 [27.0, 34.8] | 32.0 [26.9, 35.8] | 0.758 |
| Day 3 | 30.5 [27.3, 33.0] | 29.8 [26.6, 33.6] | 0.993 |
| ΔHCT | −2.1 [−4.6, 3.7] | −4.8 [−9.0, 0.3] | 0.023 |
| White blood cell | | | |
| Day 1 | 10.56 [6.10, 14.64] | 13.70 [7.34, 18.75] | 0.048 |
| Day 2 | 10.32 [7.07, 15.09] | 12.26 [8.02, 16.31] | 0.262 |
| Day 3 | 9.52 [7.88, 14.84] | 11.72 [7.75, 15.83] | 0.265 |
| ΔWBC | 0.29 [−2.89, 3.21] | −1.32 [−4.74, 1.97] | 0.136 |
| Lymphocyte | | | |
| Day 1 | 0.60 [0.36, 0.87] | 0.92 [0.49, 1.42] | 0.005 |
| Day 2 | 0.52 [0.36, 1.09] | 0.86 [0.60, 1.41] | <0.001 |
| Day 3 | 0.52 [0.37, 0.72] | 0.89 [0.55, 1.24] | <0.001 |
| ΔLym | −0.02 [−0.49, 0.39] | −0.13 [−0.46, 0.09] | 0.036 |
| Platelet | | | |
| Day 1 | 111 [73, 187] | 144 [104, 204] | 0.038 |
| Day 2 | 100 [65, 169] | 121 [75, 164] | 0.491 |
| Day 3 | 101 [59, 134] | 103 [71, 139] | 0.735 |
| ΔPlt | −18 [−50, 9] | −31 [−89, 0] | 0.434 |
| Albumin | | | |
| Day 1 | 28.9 [25.0, 33.2] | 31.1 [26.8, 36.1] | 0.096 |
| Day 2 | 31.8 [28.8, 34.3] | 33.5 [29.0, 37.6] | 0.030 |
| Day 3 | 32.9 [30.6, 38.6] | 35.0 [31.0, 39.1] | 0.255 |
| ΔALB | 4.0 [0, 8.3] | 2.1 [−2.0, 7.5] | 0.836 |
| Total bilirubin | | | |
| Day 1 | 12.5 [6.3, 22.1] | 13.8 [6.9, 23.5] | 0.896 |
| Day 2 | 17.5 [9.8, 27.2] | 15.0 [9.7, 26.4] | 0.554 |
| Day 3 | 19.4 [10.7, 33.6] | 18.8 [11.3, 33.2] | 0.455 |
| ΔTB | 5.0 [−5.5, 18.1] | 5.4 [−0.6, 14.1] | 0.455 |
| Creatinine | | | |
| Day 1 | 109 [73, 169] | 101 [71, 176] | 0.991 |
| Day 2 | 132 [78, 165] | 121 [79, 192] | 0.862 |
| Day 3 | 109 [76, 170] | 116 [75, 179] | 0.973 |
| ΔCr | 1 [−52, 17] | 1 [−25, 26] | 0.541 |
| Fibrinogen | | | |
| Day 1 | 4.09 [2.87, 4.78] | 3.90 [3.04, 4.69] | 0.944 |
| Day 2 | 3.92 [3.34, 4.64] | 3.95 [3.20, 4.69] | 0.995 |
| Day 3 | 4.25 [3.30, 4.71] | 4.11 [3.32, 4.77] | 0.754 |
| ΔFib | 0.36 [−0.59, 1.01] | 0.10 [−0.68, 0.94] | 0.774 |
| aPTT | | | |
| Day 1 | 38.8 [32.3, 51.9] | 41.5 [31.4, 60.3] | 0.679 |
| Day 2 | 40.1 [32.9, 46.9] | 38.7 [32.6, 51.4] | 0.609 |
| Day 3 | 41.4 [34.4, 45.0] | 38.2 [33.3, 46.9] | 0.760 |
| ΔaPTT | 1.8 [−13.0, 10.1] | −1.1 [−24.3, 6.9] | 0.266 |
| D-dimer | | | |
| Day 1 | 2,904 [1,196, 5,946] | 2,234 [699, 5,402] | 0.298 |
| Day 2 | 2,905 [1,212, 4,893] | 2,440 [879, 5,070] | 0.404 |
| Day 3 | 2,248 [1,090, 4,273] | 2,202 [961, 3,665] | 0.796 |
| ΔD-dimer | −76 [−2,065, 2,129] | 123 [−2194, 1,859] | 0.863 |

ΔHB, difference of hemoglobin between day 3 and day 1; ΔHCT, difference of hematocrit between day 3 and day 1; ΔWBC, difference of white blood cell count between day 3 and day 1; ΔLym, difference of lymphocyte count between day 3 and day 1; ΔPlt, difference of platelet count between day 3 and day 1; ΔALB, difference of albumin between day 3 and day 1; ΔTB, difference of total bilirubin between day 3 and day 1; ΔCr, difference of creatinine between day 3 and day 1; ΔFib, difference of fibrinogen between day 3 and day 1; aPTT, activated partial thromboplastin time; ΔaPTT, difference of aPTT between day 3 and day 1; ΔD-dimer, difference of D-dimer between day 3 and day 1.


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**Table S6** Logistic regression analysis of risk factors associated with ECMO-related infection

| Factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.013 (0.990, 1.036) | 0.279 | – | – |
| Gender† | 1.197 (0.548, 2.615) | 0.651 | – | – |
| Support type† | | | | |
| Veno-venous ECMO | Reference | | – | – |
| Veno-arterial ECMO | 0.451 (0.220, 0.925) | 0.030 | – | – |
| Immunocompromised status† | 2.870 (1.084, 7.597) | 0.034 | – | – |
| SOFA score | 1.112 (1.006, 1.229) | 0.038 | – | – |
| Broad-spectrum antibiotics before ECMO cannulation† | 3.580 (1.763, 7.266) | <0.001 | – | – |
| ECMO duration (days) | 1.204 (1.113, 1.302) | <0.001 | 1.207 (1.096, 1.330) | <0.001 |
| MV duration (days) | 1.053 (1.025, 1.082) | <0.001 | – | – |
| RRT during ECMO† | 1.875 (0.932, 3.771) | 0.078 | – | – |
| Decrease in neutrophil count† | 0.451 (0.208, 0.977) | 0.044 | – | – |
| Decrease in lymphocyte count† | 4.375 (2.097, 5.128) | <0.001 | 3.578 (2.175, 4.906) | <0.001 |

†, analyzed as categorical variables. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; RRT, renal replacement therapy; OR, odds ratio; CI, confidence interval.

**Table S7** Logistic regression analysis of risk factors associated to 90-day mortality

| Factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.032 (1.010, 1.055) | 0.003 | 1.039 (1.011, 1.068) | 0.006 |
| Gender† | 1.039 (0.529, 2.039) | 0.912 | – | – |
| Immunocompromised status† | 5.544 (1.553, 9.794) | 0.008 | – | – |
| SOFA score | 1.205 (1.093, 1.329) | <0.001 | 1.154 (1.021, 1.305) | 0.022 |
| Diabetes mellitus† | 2.569 (1.064, 6.206) | 0.036 | – | – |
| Broad-spectrum antibiotics before ECMO cannulation† | 1.749 (0.951, 3.220) | 0.072 | – | – |
| ECMO duration (days) | 1.084 (1.017, 1.156) | 0.013 | – | – |
| RRT during ECMO† | 4.895 (2.572, 9.318) | <0.001 | 4.632 (2.055, 0.444) | <0.001 |
| ECMO-related infection† | 9.743 (3.853, 24.639) | <0.001 | 4.208 (3.197, 6.524) | <0.001 |
| Decline in lymphocyte count† | 2.768 (1.490, 5.140) | 0.001 | – | – |

†, analyzed as categorical variables. SOFA, Sequential Organ Failure Assessment; ECMO, extracorporeal membrane oxygenation; RRT renal replacement therapy; OR, odds ratio; CI, confidence interval.


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**Table S8** Logistic regression analysis of risk factors associated to ECMO-related infection in patients receiving veno-venous ECMO

| Factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.021 (0.989, 1.053) | 0.196 | – | – |
| Gender† | 1.239 (0.473, 3.243) | 0.662 | – | – |
| Immunocompromised status† | 1.833 (0.644, 5.218) | 0.256 | – | – |
| SOFA score | 1.060 (0.938, 1.197) | 0.349 | – | – |
| Broad-spectrum antibiotics before ECMO cannulation† | 2.000 (0.780, 5.127) | 0.149 | – | – |
| ECMO duration (days) | 1.141 (1.050, 1.240) | 0.002 | 1.124 (1.017, 1.242) | 0.022 |
| MV duration (days) | 1.045 (1.013, 1.079) | 0.005 | – | – |
| RRT during ECMO† | 2.687 (1.114, 6.481) | 0.028 | – | – |
| Decline in neutrophil count† | 0.444 (0.162, 1.221) | 0.116 | – | – |
| Decline in lymphocyte count† | 4.390 (2.157, 6.465) | <0.001 | 3.095 (1.732, 5.580) | 0.003 |

†, analyzed as categorical variables. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; RRT renal replacement therapy; OR, odds ratio; CI, confidence interval.

**Table S9** Logistic regression analysis of risk factors associated to ECMO-related infection in patients receiving veno-arterial ECMO

| Factors | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.004 (0.968, 1.042) | 0.827 | – | – |
| Gender† | 1.248 (0.309, 5.047) | 0.756 | – | – |
| SOFA score | 1.279 (1.053, 1.555) | 0.013 | 1.649 (1.160, 2.343) | 0.005 |
| Broad-spectrum antibiotics before ECMO cannulation† | 3.700 (2.149, 5.216) | 0.002 | – | – |
| ECMO duration (days) | 1.483 (1.170, 1.880) | 0.001 | 1.858 (1.243, 2.778) | 0.003 |
| MV duration (days) | 1.065 (0.998, 1.136) | 0.059 | – | – |
| RRT during ECMO† | 1.264 (0.380, 4.211) | 0.702 | – | – |
| Decline in neutrophil count† | 0.525 (0.153, 1.799) | 0.305 | – | – |
| Decline in lymphocyte count† | 2.390 (1.364, 4.930) | 0.019 | 1.526 (1.006, 2.313) | 0.049 |

†, analyzed as categorical variables. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; RRT renal replacement therapy; OR, odds ratio; CI, confidence interval.


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**Table S10** Logistic regression analysis of risk factors associated to ECMO-related infection in patients whose lymphocyte count on day 1 greater than or equal to $1.0\times10^9$/L

| Factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.017 (0.975, 1.061) | 0.440 | – | – |
| Support type† | | | | |
| Veno-venous ECMO | Reference | | – | – |
| Veno-arterial ECMO | 0.545 (0.136, 2.187) | 0.392 | – | – |
| SOFA score | 1.097 (0.895, 1.345) | 0.374 | – | – |
| Broad-spectrum antibiotics before ECMO cannulation† | 3.333 (0.793, 4.010) | 0.100 | – | – |
| Immunocompromised status | 2.555 (0.376, 4.375) | 0.197 | – | – |
| ECMO duration (days) | 1.112 (0.970, 1.274) | 0.129 | – | – |
| MV duration (days) | 1.031 (0.997, 1.067) | 0.076 | – | – |
| RRT during ECMO† | 2.667 (0.521, 6.655) | 0.116 | – | – |
| Decline in neutrophil count† | 0.452 (0.112, 1.821) | 0.264 | – | – |
| Decline in lymphocyte count† | 3.874 (0.938, 6.090) | 0.057 | 2.691 (0.876, 5.717) | 0.064 |

†, analyzed as categorical variables. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; RRT renal replacement therapy; OR, odds ratio; CI, confidence interval.

**Table S11** Logistic regression analysis of risk factors associated to ECMO-related infection in patients whose lymphocyte count on day 1 less than $1.0\times10^9$/L

| Factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.004 (0.975, 1.033) | 0.812 | – | – |
| Gender† | 0.947 (0.392, 2.283) | 0.903 | – | – |
| Support type† | | | | |
| Veno-venous ECMO | Reference | | – | – |
| Veno-arterial ECMO | 0.737 (0.286, 1.901) | 0.528 | – | – |
| SOFA score | 1.124 (0.998, 1.267) | 0.054 | – | – |
| Broad-spectrum antibiotics before ECMO cannulation† | 2.600 (1.089, 6.209) | 0.031 | – | – |
| Immunocompromised status | 1.873 (0.653, 5.370) | 0.243 | – | – |
| ECMO duration (days) | 1.214 (1.104, 1.335) | <0.001 | 1.167 (1.007, 1.351) | 0.039 |
| MV duration (days) | 1.070 (1.029, 1.114) | 0.001 | – | – |
| RRT during ECMO† | 2.245 (0.9831, 5.128) | 0.055 | – | – |
| Decline in neutrophil count† | 0.471 (0.182, 1.214) | 0.119 | – | – |
| Decline in lymphocyte count† | 5.067 (2.875, 9.369) | 0.057 | 4.883 (3.087, 8.357) | 0.001 |

†, analyzed as categorical variables. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; RRT renal replacement therapy; OR, odds ratio; CI, confidence interval.


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**Table S12** Logistic regression analysis of risk factors associated to ECMO-related infection (exclude immunocompromised patients)

| Factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age (years) | 1.008 (0.984, 1.033) | 0.525 | – | – |
| Gender† | 0.879 (0.390, 1.984) | 0.757 | – | – |
| Support type† | | | | |
| Veno-venous ECMO | Reference | | – | – |
| Veno-arterial ECMO | 0.473 (0.220, 1.017) | 0.055 | – | – |
| SOFA score | 1.149 (1.029, 1.284) | 0.014 | – | – |
| Broad-spectrum antibiotics before ECMO cannulation† | 3.742 (1.730, 8.093) | 0.001 | – | – |
| ECMO duration (days) | 1.202 (1.102, 1.312) | <0.001 | 1.124 (1.017, 1.242) | 0.022 |
| MV duration (days) | 1.049 (1.021, 1.078) | <0.001 | – | – |
| RRT during ECMO† | 1.846 (0.859, 3.969) | 0.116 | – | – |
| Decline in neutrophil count† | 0.449 (0.187, 1.075) | 0.072 | – | – |
| Decline in lymphocyte count† | 4.380 (1.939, 7.896) | <0.001 | 3.095 (1.732, 5.580) | 0.003 |

†, analyzed as categorical variables. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; RRT renal replacement therapy; OR, odds ratio; CI, confidence interval.


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