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Bloodstream and respiratory coinfections in patients with COVID-19 on ECMO

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Abstract

Background: Although several studies have characterized the risk of coinfection in COVID pneumonia, the risk of the bloodstream and respiratory coinfection in patients with COVID-19 pneumonia on extracorporeal membrane oxygenation (ECMO) supports severe acute respiratory distress syndrome (ARDS) is poorly understood.

Methods: This is a retrospective analysis of patients with COVID-19 ARDS on ECMO at a single center between January 2020 and December 2021. Patient characteristics and clinical outcomes were compared.

Results: Of 44 patients placed on ECMO support for COVID-19 ARDS, 30 (68.2%) patients developed a coinfection, and 14 (31.8%) patients did not. Most patients underwent venovenous ECMO (98%; 43/44) cannulation in the right internal jugular vein (98%; 43/44). Patients with coinfection had a longer duration of ECMO (34 [interquartile range, IQR: 19.5, 65] vs. 15.5 [IQR 11, 27.3] days; $p = .02$), intensive care unit (ICU; 44 [IQR: 27,75.5] vs 31 [IQR 20–39.5] days; $p = .03$), and hospital (56.5 [IQR 27,75.5] vs 37.5 [IQR: 20.5–43.3]; $p = .02$) length of stay. When stratified by the presence of a coinfection, there was no difference in hospital mortality (37% vs. 29%; $p = .46$) or Kaplan–Meier survival (logrank $p = .82$). Time from ECMO to first positive blood and respiratory culture were 12 [IQR: 3, 28] and 10 [IQR: 1, 15] days, respectively. Freedom from any coinfection was 50 (95% confidence interval: 37.2–67.2)% at 15 days from ECMO initiation.

Conclusions: There is a high rate of co-infections in patients placed on ECMO for COVID-19 ARDS. Although patients with coinfections had a longer duration of extracorporeal life support, and longer length of stays in the ICU and hospital, survival was not inferior.

KEYWORDS

coinfection, COVID-19, extracorporeal membrane oxygenation, secondary infection

Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; CRP, C-reactive protein; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; ELSO, Extracorporeal Life Support Organization; ICU, intensive care unit; IQR, interquartile range; LA, lactic acid; LDH, lactate dehydrogenase; P/F, arterial partial pressure of oxgen/fraction of inspired oxygen.

1 | INTRODUCTION

Over the last few years, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19) pandemic has continued to challenge healthcare systems worldwide. Treatment strategies for COVID-19 continue to adjust as the body of evidence grows and evolves. While bacterial and fungal coinfection has previously been reported in patients with severe influenza[1,2] and Middle East respiratory syndrome coronavirus,[3–5] its incidence and prognostic indications in patients with severe COVID-19 are not well understood.[6–8] Although rates of bacterial coinfections have been reportedly low among all COVID-19 patients (3%–14%),[7–9] several reports have demonstrated that the use of antibiotics in patients with COVID-19 is frequent.[7,8,10] This likely reflects the dilemma of astute antibiotic stewardship to avoid antimicrobial resistance and other clinical repercussions of liberal antibiotic use[11] in the face of severe COVID-19 illness with potential coinfection. The use of extracorporeal membrane oxygenation (ECMO) as rescue therapy for severe acute respiratory distress syndrome (ARDS) has been described by multiple studies throughout the pandemic.[12–19] In the 2021 updated guidelines from the Extracorporeal Life Support Organization (ELSO), the indication for use of ECMO in COVID-19 patients is described, although with more stringent contraindications and a strong recommendation for the formation of regional ECMO referral networks given the constraint on the resources from the pandemic.[20] Infectious complications on ECMO have also been associated with increased mortality and morbidity with reported increased risk of death as high as 38%–63%.[21,22] In the setting of the current pandemic, there is little known about rates of coinfection in patients with COVID-19 on ECMO for severe ARDS. The goal of this study is to describe the clinical course of patients who develop bloodstream and/or respiratory co-infections while on ECMO for COVID-19 ARDS.

2 | METHODS

2.1 | Study design

We conducted a retrospective analysis of 44 patients with laboratory-confirmed COVID-19, all of whom were treated at a single ECMO referral center from January 2020 to December 2021. The study was approved by the Institutional Review Board, and the requirement for informed consent was waived due to the retrospective nature of the study.

2.2 | Patient management

Patients were managed by multidisciplinary teams including medical and surgical intensivists, cardiothoracic surgeons, ECMO specialists, infectious disease specialists, nephrologists, and other consultants as indicated. The details of ECMO management and protocols for the management of COVID-19 patients have been described in detail previously.[23]

2.3 | Outcome measures

The primary outcome of this study was freedom from coinfection from the date of ECMO cannulation. Secondary outcomes include details of the bloodstream and respiratory cultures obtained on the patients including the total number of cultures drawn in the cohort, number of positive cultures, the average number of cultures per patient, time from ECMO cannulation to a first positive culture, number of patients with positive cultures, and patients with polymicrobial infection. Details of extracorporeal life support (ECLS) include the severity of ARDS as defined by the Berlin criteria by the arterial partial pressure of oxygen/fraction of inspired oxygen (P/F) ratio, the proportion of patients paralyzed, proned, and on vasopressors before initiation of ECLS, type of ECLS, cannulation site, time from onset of symptoms to admission and intubation, time from admission and positive COVID test date to ECLS, length of ECLS, tracheostomy, patients decannulated, death after decannulation, patients requiring recannulation, patients withdrawn from ECMO, length of stay in the intensive care unit (ICU) and hospital, hospital mortality, and discharge disposition. Additionally, survival of patients with and without coinfections was obtained as well as the micro-organisms isolated in positive blood and respiratory cultures. Subanalyses of trends in inflammatory markers including lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, and lactic acid (LA) within a 5-day time window of 2 days before and after positive blood and respiratory cultures were performed.

2.4 | Statistical analysis

Continuous variables were presented as the mean ± standard deviation or median with interquartile range (IQR) as appropriate, and categorical variables as proportions, unless otherwise specified. Depending on the type of data, Student's *t*-test, unequal variance *t*-test, Mann–Whitney *U* test, Fisher's exact test, or χ^2 test were used to evaluate differences in the two groups. Kaplan–Meier analysis was used with the logrank test to determine differences in survival rates between the two groups. $p < .05$ was considered statistically significant, and no adjustments were made for multiple comparisons. The differences in the repeated measurements of levels of the inflammatory markers within a 5-day window of a positive test for coinfection were detected using the Friedman test. All statistical analyses were performed using RStudio (Version 4.0.0).

TABLE 1 Demographics and comorbidities of patients who underwent extracorporeal membrane oxygenation for COVID-19

	Overall (n = 44)	Coinfection (n= 30)	No coinfection (n= 14)	p-Value
Age (year)	48 [41, 51.3]	48 [42.5, 51]	48.5 [41, 54.8]	.95
Male	33 (75)	24 (80)	9 (64)	.26
Race				
White	16 (36)	9 (30)	7 (50)	.20
Black	7 (16)	3 (10)	4 (29)	.12
Hispanic	18 (41)	15 (50)	3 (21)	.07
Other	3 (7)	3 (10)	0 (0)	.22
BMI (kg/m^2)	33.1 ± 5.8	33.2 ± 5.4	33.0 ± 6.7	.92
HTN	17 (39)	12 (40)	5 (36)	.79
DM	8 (18)	5 (17)	3 (21)	.70
HLD	12 (27)	9 (30)	3 (21)	.55
COPD	1 (2)	0 (0)	1 (7)	.13
Active smoker	2 (5)	2 (7)	0 (0)	.32
Malignancy	2 (5)	1 (3)	1 (7)	.57
CAD	1 (2)	1 (3)	0 (0)	.49
Hemodialysis	2 (5)	1 (3)	1 (7)	.57
Immunocompromised	1 (2)	0 (0)	1 (7)	.14

Note: Categorical variables as n (%), continuous variables as mean ± SD or median [IQR]. p-values compare statistical significance between patients with coinfection and no coinfection.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; IQR, interquartile range.

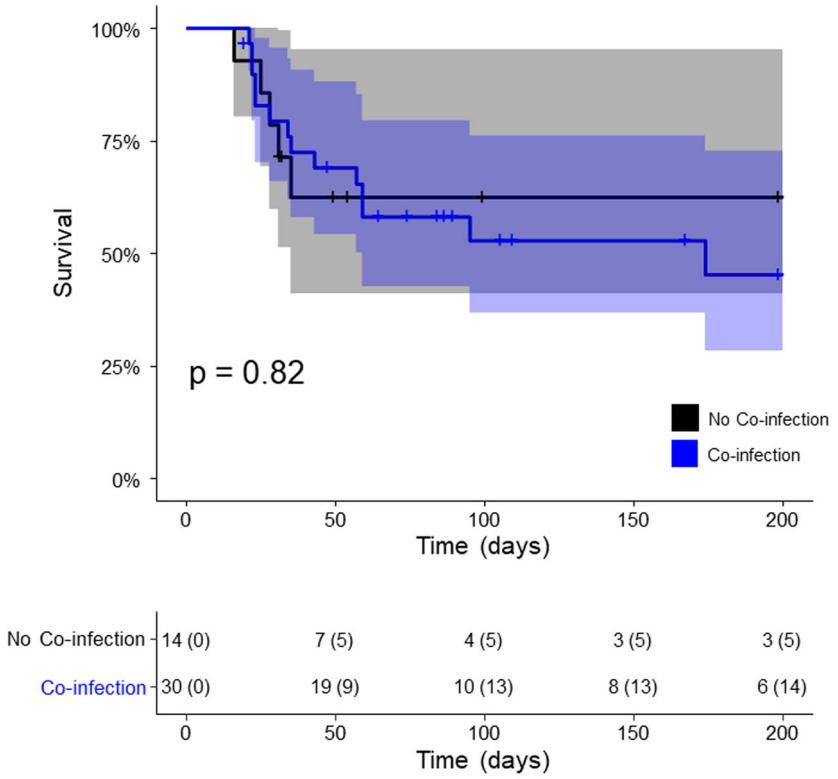

FIGURE 1 Kaplan–Meier survival in patients on ECMO for COVID with coinfection versus no coinfection. The black line delineates patients who did not develop a coinfection while on ECMO, the blue line delineates patients who developed a coinfection. Shaded areas represent 95% confidence intervals. ECMO, extracorporeal membrane oxygenation.

TABLE 2 Details of ECLS

	Overall ($n = 44$)	Coinfection ($n = 30$)	No coinfection ($n = 14$)	p-Value
Pre-ECLS P/F ratio	67 [58.8, 88.3]	65 [52, 83]	71 [62, 93]	0.20
Paralyzed	44 (100)	30 (100)	14 (100)	1.0
Prone	29 (66)	21 (70)	8 (57)	0.40
Vasopressors	7 (16)	7 (23)	0 (0)	0.05
Type of ECLS				
VV	43 (98)	29 (97)	100 (0)	0.49
VA	1 (2)	1 (3)	0 (0)	0.49
Initial cannulation site				
RIJ	43 (98)	29 (97)	100 (0)	0.49
Bifemoral	1 (2)	1 (3)	0 (0)	0.49
Onset of symptoms to admission	7 [4, 10]	9 [6, 12]	1 [0, 6]	<0.01
Onset of symptoms to intubation	12.5 [8.3, 20.8]	16.5 [11.5, 23]	7 [1.8, 13.8]	0.01
Admission to ECLS	9 [4.8, 14]	9.5 [5.5, 14]	8 [4.5, 12.5]	0.82
Positive COVID test date to ECLS	13 [8.3, 20]	16 [9, 21]	10 [7.3, 16]	0.15
Duration of ECLS (d)	24 [12.5, 56.3]	34 [19.5, 65]	15.5 [11, 27.3]	0.02
Tracheostomy	35 (80)	26 (87)	9 (64)	0.09
Decannulated	27 (61)	17 (57)	10 (71)	0.35
Recannulation	3 (7)	3 (10)	0 (0)	0.22
Death after decannulation	1 (2)	0 (0)	1 (7)	0.14
Withdrawn from ECMO	15 (34)	11 (37)	4 (29)	0.60
Length of stay in ICU (d)	39 [25, 65]	44 [27, 75.5]	31 [20–39.5]	0.03
Length of stay in hospital (d)	42.5 [26.8, 73.3]	56.5 [27, 75.5]	37.5 [20.5–43.3]	0.02
Hospital mortality	15 (39)	11 (37)	4 (29)	0.46
Discharge disposition ($n = 27$)				
Home	2 (7.4)	1 (6)	1 (10)	0.66
LTAC	9 (33.3)	7 (39)	2 (20)	0.31
Transferred to another Hospital	16 (59.3)	10 (56)	6 (60)	0.82

Note: Categorical variables as n (%), continuous variables as mean ± SD or median [IQR]. p-values compare statistical significance between patients with coinfection and no coinfection.

Abbreviations: ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; LTAC, long-term assisted care; P/F, arterial partial pressure of oxygen/fraction of inspired oxygen; RIJ, right internal jugular; VA, venoarterial; VV, venovenous.

3 | RESULTS

3.1 | Patients

There were 44 patients who were placed on ECMO support for COVID-19 ARDS between January 2020 and December 2021, of which 30 (68.2%) patients developed a coinfection, and 14 (31.8%) patients did not develop coinfection. The median age of the cohort was 48 (IQR: 41, 51.3) years, and 75% (33/44) of patients were male. Most patients were of Hispanic ethnicity (41%; 18/44). The average body mass index was 33.1 ± 5.8 kg/m^2 and the most common comorbidity was hypertension (39%; 17/44). The demographics and comorbidities between patients who did and did not develop coinfection were similar (Table 1).

3.2 | Details of ECLS

Before initiation of ECMO, all patients in our cohort were paralyzed, 29 (66%) were proned, and 7 (16%) required

TABLE 3 Coinfection

	Overall (*n* = 44)
Bloodstream cultures	
Number obtained	369
Number positive, (% out of obtained)	67 (18.2)
The median number is drawn per patient	7 [4, 11.5]
Time from ECLS to first positive culture (d)	12 [3, 28]
Patients with positive culture(s)	19 (43.2)
Patients with polymicrobial infection	7 (15.9)
Respiratory cultures	
Number obtained	135
Number positive, (% out of obtained)	71 (52.6)
The median number is drawn per patient	3 [1,4.3]
Time from ECLS to first positive culture (d)	10 [1, 15]
Patients with positive culture(s)	26 (59.1)
Patients with polymicrobial infection	13 (29.5)
Patients with positive blood and respiratory cultures	15 (34.1)
Time from admission to initiation of antibiotics (d)	10 [5.8–15.3]
Duration of antibiotics (d)	28 [14.8–59.3]

Note: Categorical variables as *n* (%), continuous variables as median [IQR].
Abbreviations: ECLS, extracorporeal life support; IQR, interquartile range.

vasopressor support. The mean P/F ratio was 67 (IQR: 58.8, 88.3). Almost all patients underwent venovenous ECMO (98%; 43/44) and were initially cannulated in the right internal jugular vein under echocardiographic guidance (98%; 43/44). The median time from reported onset of symptoms to admission (9 [IQR: 6, 12] vs. 1 [IQR: 0, 6] days; $p < .01$) and intubation (16.5 [IQR: 11.5, 23] vs. 7 [IQR: 1.8, 13.8] days; $p = .01$) were longer in patients who developed a coinfection on ECMO. The median time from admission to initiation of ECMO was 13 [IQR: 8.3–20] days and was similar between the two groups. However, patients who developed a coinfection had a longer average duration of ECLS (34 [IQR: 19.5, 65] vs. 15.5 [IQR: 11, 27.3] days; $p = .02$). Most patients underwent tracheostomy (80%; 35/44). There were 25 (57%) patients who underwent ECMO decannulation and 3 (7%) who required recannulation. One (2%) patient died after decannulation, and 15 (34%) were withdrawn from ECMO. There was one (2%) patient who was transferred on ECMO to another facility for bilateral lung transplant evaluation. Patients who developed a coinfection had a longer median length of stay in the ICU (44 [IQR: 27, 75.5] vs. 31 [IQR: 20–39.5] days; $p = .03$), and hospital (56.5 [IQR: 27, 75.5] vs. 37.5 [IQR: 20.5–43.3]; $p = .02$). However, hospital mortality was similar between patients who did and did not develop a coinfection (37% vs. 29%; $p = .46$). Kaplan–Meier survival in the overall cohort was 79.2 (95% confidence interval [CI]: 67.9–92.3)% at 30 days, 54.4 (95% CI: 40.4–73.2)% at 100 days, and 48.9 (95% CI: 34.1–70.3)% at 200 days. There was no difference in survival between patients who developed a coinfection and those who did not out to 200 days (logrank $p = .82$) (Figure 1). Of the 27 patients discharged alive, 59.3% (16/27) were transferred back to the referring hospital for additional ventilatory management once ECMO was no longer indicated, 33.3% (9/27) were discharged to a long-term assisted care facility, and 7.4% (2/27) were discharged home (Table 2).

3.3 | Bloodstream and respiratory coinfections

There were 369 blood cultures obtained among our cohort of patients, of which 18.2% (67/369) were positive results. The median number of blood cultures drawn per patient was 7 (4, 11.5). There were 19 (43.2%) patients with one or more positive blood culture result(s), and 7 (15.9%) patients with polymicrobial infections. The median time from initiation of ECMO to the first positive blood culture was 12[3,24] days (Table 3). The most common organism present in positive blood culture samples was *Enterococcus faecalis*, followed by *Candida species*, *Staphylococcus epidermidis*, and methicillin-resistant *Staphylococcus aureus*. The breakdown of micro-organisms isolated from positive blood culture samples is represented in Figure 2.

A total of 135 respiratory cultures were obtained among our cohort of patients, of which 52.6% (71/135) were positive. The median number of respiratory cultures drawn per patient was 3 (1, 4.3). There were 26 (59.1%) patients with positive respiratory culture(s), and 13 (29.5%) patients with a polymicrobial infection. The median time from initiation of ECMO to the first positive respiratory culture was 10[1,15] days. The most common organism present in positive respiratory culture samples was methicillin-resistant *Staphylococcus aureus*, followed by *Pseudomonas aeruginosa*, and *Candida species* (Figure 3).

There were 15 (34.1%) patients with positive blood and respiratory cultures. All patients in the cohort were treated with intravenous antibiotics. The most common antibacterial agents utilized were vancomycin (89%; 39/44), penicillin base± beta-lactamase inhibitor (82%; 36/44), cephalosporin 73% (32/44), and aminoglycoside (45%; 20/44). The details of antibacterial, antifungal, and antiviral agents utilized are detailed in Table 4. The median time from admission to initiation of antibiotics was 10 (5.8–15.3) days. The median duration of antibiotic treatment was 28 (14.8–59.3) days.

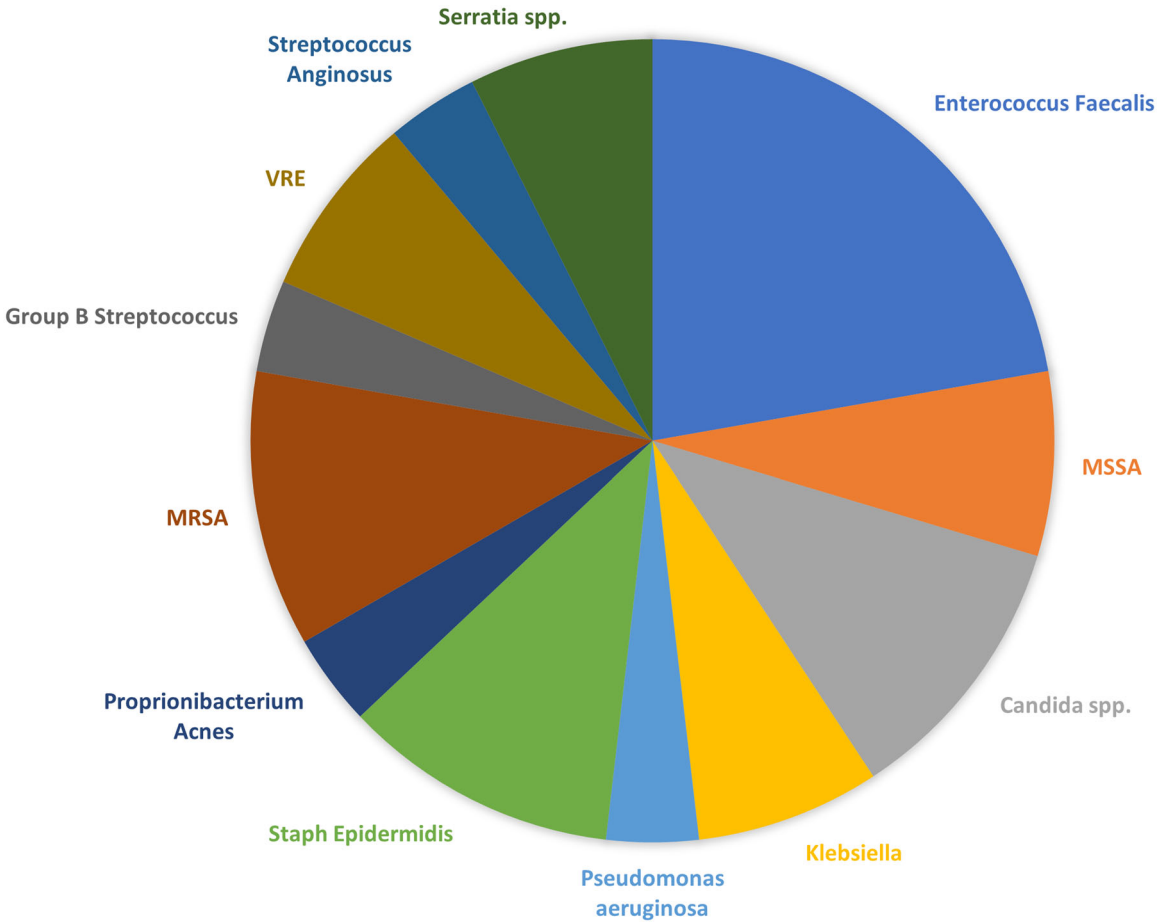

FIGURE 2 Microorganisms present in positive bloodstream cultures in patients on ECMO for COVID-19. The most common bloodstream infection was *Enterococcus faecalis* followed by *Staphylococcus* infections. ECMO, extracorporeal membrane oxygenation; MRSA, methicillin-resistent *Staphylococcus aureus*; MSSA methicillin-sensitive *Staphylococcus aureus*; spp, species; VRE, vancomycin-resistant enterococcus.

A Kaplan–Meier analysis was used to estimate the freedom of coinfection represented in Figure 4. Freedom from any coinfection was 50% (37.2%–67.2%) at 15 days from ECMO initiation. Freedom from bloodstream coinfection was less than 50% (48.1 [33.6–68.7]%) at 62 days, and at 27 days for respiratory coinfection (49.5% [36.6–66.9]%).

3.4 | Inflammatory markers

The trends of inflammatory markers within a 5-day time window of 2 days before and after the date of each patient's first positive blood culture showed increasing LDH and CRP levels; however, these were not statistically significant (LDH $p = .85$, CRP $p = .33$) (Supporting Information: Figure 1A). There was no noticeable trend in ferritin ($p = .17$) or LA ($p = .25$) (Supporting Information: Figure 1B). There was similarly no significant association between trends in inflammatory markers with respect to the date of a first positive respiratory culture in our cohort.

4 | COMMENT

The rate and prognostic indications of co-infection in patients on ECMO support for COVID-19 ARDS are not known. To the authors' knowledge, this is the first report to describe the incidence of coinfection in this population of patients. In our cohort, the rate of coinfection was significantly higher than previously reported in patients with COVID-19 who did not require ECMO.[7–10] Most notably, more than 50% of patients developed either a bloodstream or respiratory coinfection by Day 15 of ECLS initiation with increasing rates over time. Although patients who developed a coinfection had a longer duration of ECLS and length of stay in the ICU and hospital, survival was similar to patients who did not develop a co-infection.

The incidence of coinfection in patients with severe COVID-19 infection has been historically low. A meta-analysis of 30 studies including over 3000 patients describing coinfections found that the overall pooled proportion of patients with bacterial coinfections was 7%, and 14% in a subanalysis only

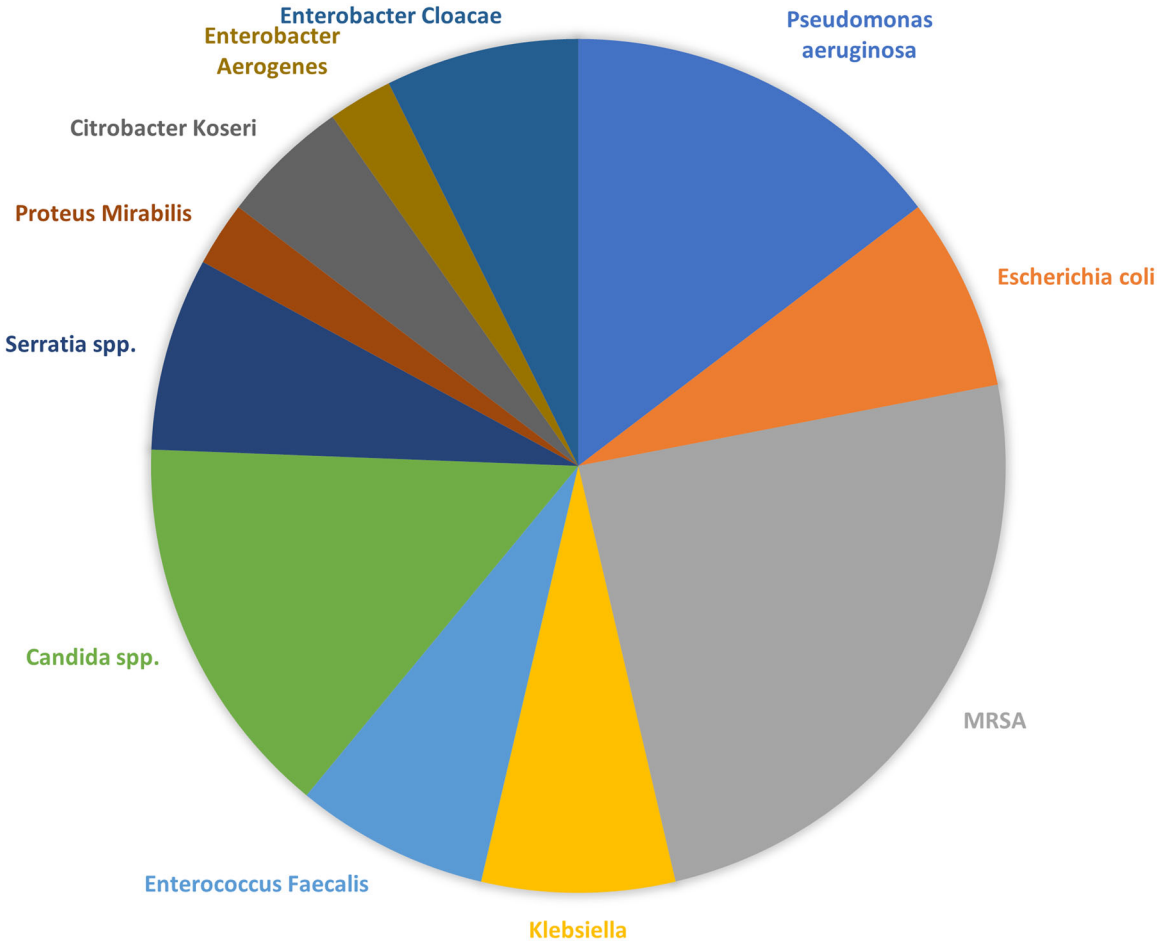

FIGURE 3 Microorganisms present in positive respiratory cultures in patients on ECMO for COVID-19. The most common organism in respiratory infections was methicillin-resistant *Staphylococcus aureus* (MRSA) followed by *Pseudomonas aeruginosa*. ECMO, extracorporeal membrane oxygenation; spp, species.

including ICU patients.[7] Another large multicenter study in the UK similarly showed a 3.2% rate of bacterial and 13.3% rate of respiratory coinfection in patients with COVID-19.[9] These rates are significantly lower than the nearly 70% coinfection rate that was observed in patients on ECMO for COVID-19 ARDS our study. The study from the UK also noted that patients with COVID-19 and secondary bacteremia had an increased risk of death compared to baseline admitted patients (relative risk: 1.51); however, this was not reflected in patients with a respiratory coinfection (relative risk: 0.90).[9] In our series, it is notable that with diligent critical care by a multidisciplinary specialist team, the survival of patients who developed a bloodstream and/or respiratory coinfection was not inferior. In fact, the overall hospital mortality in our series was 39%, which is consistent with the 37% hospital mortality 90 days after ECMO initiation reported by the ELSO registry for patients cannulated after May 1st, 2020.[25]

Secondary infection is a known complication of ECMO therapy. This could be in part due to the high number of catheters that are placed in ECMO patients, including the ECMO cannulas themselves, central venous catheters, and peripheral arterial catheters.[26] Furthermore, patients are more likely to have risk factors for bloodstream infections, such as anemia and thrombocytopenia requiring blood product transfusions[27] or renal failure.[28] Two reviews of the ELSO registry reported a prevalence of hospital-acquired infections during ECMO to be 21% in adults.[21,22] Several studies have also identified increased duration of ECMO as a risk factor for developing a secondary infection.[24,29–31] In a retrospective analysis of 334 patients on ECMO, the rate of bloodstream infections at 20–30 days was about 25%. The study also identified a longer duration of ECMO to be associated with mortality.[31] In our series, more than 50% of patients on ECMO for COVID-19 developed coinfection by 30 days after ECMO initiation. Our data showed that patients were

TABLE 4 Antibacterial, antifungal, and antiviral agents utilized

Antibacterial	Overall (*n* = 44)
Vancomycin	39 (89)
Penicillin class ± beta-lactamase inhibitor	36 (82)
Cephalosporin	32 (73)
Aminoglycoside	20 (45)
Carbapenem	16 (36)
Daptomycin	5 (11)
Fluoroquinolone	4 (9)
Tetracycline	4 (9)
Macrolide	4 (9)
Metronidazole	4 (9)
Trimethoprim/sulfamethoxazole	3 (7)
Lincosamide	1 (2)
Rifampin	1 (2)
Antifungal	
Echinocandin	21 (48)
Ergosterol inhibitor	3 (7)
Amphotericin	2 (5)
Triazole	1 (2)
Antiviral	
Guanosine analogue	8 (18)
Remdesivir	9 (20)

Note: Values are presented as *n* (%).

more likely to develop respiratory coinfections earlier and more frequently compared to bloodstream infections. However, patients had similar survival regardless of whether they developed a coinfection. In another observational study from Australia, a longer duration of ECMO was also independently associated with the risk of bloodstream infection with the most frequent pathogen being *Enterobacteriaceae*.[30] Our study similarly showed that *Enterococcus faecalis* was the most common organism found in bloodstream coinfections. Studies have hypothesized that patients on systemic circulatory support may affect gut permeability, which could increase the risk of bacterial and fungal translocation.[32,33] Furthermore, patients who developed a coinfection comparatively had a longer duration of ECLS as well as longer stays in the ICU and hospital in our series.

Antibiotic prophylaxis during ECMO is common despite a paucity of studies justifying this practice. A survey of ECLS directors of institutions in the United States belonging to the ELSO registry revealed that half of participating centers routinely prescribed antimicrobial prophylaxis for patients on ECMO.[34] In addition, a third of institutions sent daily blood cultures as part of routine surveillance.[34] In this cohort, the majority of patients were initiated on vancomycin and either cephalosporin or penicillin class antibiotics at the time of ECMO initiation. The optimal pharmacologic treatment for SARS-CoV-2 illness has continued to evolve since the pandemic. While the dangers of overzealous antimicrobial use must be considered, it is still common practice at this institution to initiate patients on empiric antibiotics at the time of ECMO cannulation due to the critical and rapidly deteriorating clinical status of patients. Interestingly, patients in our series who developed a coinfection had a longer length of time from the onset of symptoms to admission and intubation. Future studies are needed to consider potentially limiting empiric antimicrobial treatment for patients on ECMO for COVID-19 who were intubated 2 or more weeks from the onset of reported symptoms.

4.1 | Limitations

This study is subject to limitations inherent to all retrospective studies. In addition, the cohort of patients was acquired from a single ECMO referral center, so the generalizability of the findings is unknown. This study also does not account for the effect of positive urine cultures or viral coinfections on this patient group. In addition, this is a small size cohort. Along with the incomplete inflammatory marker levels around the date of positive cultures, this is likely the cause of insignificant trends in the subanalysis. Further studies with larger cohorts are needed to investigate the predictive value of trends in inflammatory markers with the development of coinfections in COVID-19. Lastly, the follow-up information after discharge in this series is limited. Further studies evaluating the quality of life after discharge of patients who survive the acute phase of ECMO support for COVID-19 and coinfection are needed.

5 | CONCLUSION

In this report, we found that there was a high rate of coinfections in patients placed on ECMO for COVID-19 ARDS. Patients who developed coinfections had a longer duration of ECLS and longer length of stays in the ICU and hospital. However, the survival of patients with coinfection was not inferior to careful and attentive ICU care from a multidisciplinary team. Further studies with larger cohorts are needed to confirm these findings

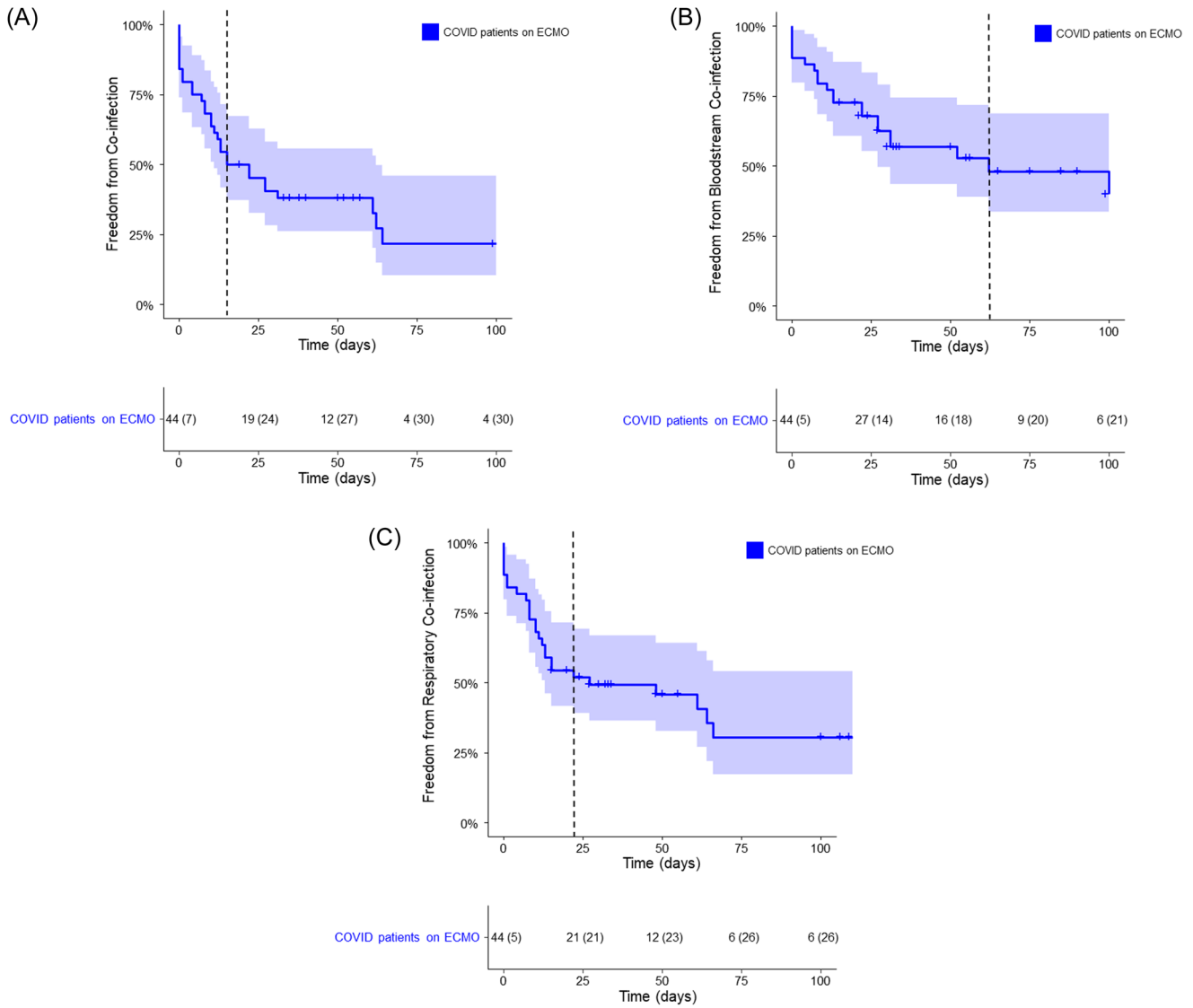

FIGURE 4 Kaplan–Meier analysis freedom from coinfection from time of ECMO cannulation in patients with COVID-19. Shaded areas represent the 95% confidence interval. Dashed lines represent the point at which freedom from an event is 50%. (A) Freedom from any coinfection. On Day 15 from ECMO cannulation, freedom from coinfection is 50 [37.2–67.2]%. (B) Freedom from bloodstream coinfection. On Day 62 from ECMO cannulation, freedom from coinfection is 48.1 (33.6–68.7]%. (C) Freedom from respiratory coinfection. On Day 27 from ECMO cannulation, freedom from coinfection is 49.5 (36.6–66.9)%. ECMO, extracorporeal membrane oxygenation.

and address the efficacy of antibiotic prophylaxis in this patient population.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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