A Daily, Respiratory Therapist Assessment of Readiness to Liberate From Venovenous Extracorporeal Membrane Oxygenation in Patients With Acute Respiratory Distress Syndrome

OBJECTIVES: We assessed the effect of implementing a protocol-directed strategy to determine when patients can be liberated from venovenous extracorporeal membrane oxygenation on extracorporeal membrane oxygenation duration, time to initiation of first sweep-off trial, duration of mechanical ventilation, ICU length of stay, hospital length of stay, and survival to hospital discharge.

DESIGN: Single-center retrospective before and after study.

SETTING: The medical ICU at an academic medical center.

PATIENTS: One-hundred eighty patients with acute respiratory distress syndrome managed with venovenous extracorporeal membrane oxygenation at a single institution from 2013 to 2019.

INTERVENTIONS: In 2016, our institution implemented a daily assessment of readiness for a trial off extracorporeal membrane oxygenation sweep gas (“sweep-off trial”). When patients met prespecified criteria, the respiratory therapist performed a sweep-off trial to determine readiness for discontinuation of venovenous extracorporeal membrane oxygenation.

MEASUREMENTS AND MAIN RESULTS: Sixty-seven patients were treated before implementation of the sweep-off trial protocol, and 113 patients were treated after implementation. Patients managed using the sweep-off trial protocol had a significantly shorter extracorporeal membrane oxygenation duration (5.5 d [3–11 d] vs 11 d [7–15.5 d]; \( p < 0.001 \)), time to first sweep-off trial (2.5 d [1–5 d] vs 7.0 d [5–11 d]; \( p < 0.001 \)), duration of mechanical ventilation (15.0 d [9–31 d] vs 25 d [21–33 d]; \( p = 0.017 \)), and ICU length of stay (18 d [10–33 d] vs 27.0 d [21–36 d]; \( p = 0.008 \)). There were no observed differences in hospital length of stay or survival to hospital discharge.

CONCLUSIONS: In patients with acute respiratory distress syndrome managed with venovenous extracorporeal membrane oxygenation at our institution, implementation of a daily, respiratory therapist assessment of readiness for a sweep-off trial was associated with a shorter time to first sweep-off trial and shorter duration of extracorporeal membrane oxygenation. Among survivors, the postassessment group had a reduced duration of mechanical ventilation and ICU lengths of stay. There were no observed differences in hospital length of stay or inhospital mortality.

KEY WORDS: acute respiratory distress syndrome; duration of treatment; extracorporeal membrane oxygenation; hospital respiratory therapy department; length of stay
Venovenous extracorporeal membrane oxygenation (ECMO) is commonly used as a rescue strategy for acute respiratory failure, including acute respiratory distress syndrome (ARDS) (1, 2). Although the use of venovenous ECMO has expanded, there is currently no standard practice to assess an individual patient’s readiness to liberate from extracorporeal support. The weaning process varies greatly between individual institutions and may not be standardized across patients within an institution (3–6). Large, randomized clinical trials investigating the use of venovenous ECMO for ARDS have left the timing of ECMO discontinuation largely to clinician discretion (7, 8).

Multiple prospective randomized trials have demonstrated that in mechanically ventilated patients, protocol-directed, daily spontaneous breathing trials (SBTs) lead to a shorter duration of mechanical ventilation and ICU length of stay (LOS) (9–11). Daily sedation interruptions or spontaneous awakening trials (SATs) in mechanically ventilated patients shorten the duration of mechanical ventilation, ICU LOS, and hospital LOS (12, 13). When paired together, daily SAT/SBTs lead to a decreased overall likelihood of death (14).

Building on these principles, in 2016, our institution adopted a daily, protocol-directed, respiratory therapist (RT)-ECMO specialist performed assessment for readiness to liberate from venovenous ECMO. This protocol allowed the RT-ECMO specialist to independently initiate a “sweep-off trial” (SOT) when specified criteria were met. We retrospectively analyzed our center’s outcomes for patients with ARDS treated with venovenous ECMO before and after implementing this daily, protocol-directed ECMO weaning strategy.

MATERIALS AND METHODS

Study Design

We performed a retrospective, uncontrolled before and after study to assess the impact of implementing a protocol-directed ECMO weaning strategy on patients with ARDS treated with venovenous ECMO. The Duke University Health System Institutional Review Board (IRB) approved the study prior to data collection and waived the need for informed consent (IRB Number: Pro00090196). Data were collected by review of the electronic medical records of all patients with ARDS treated with venovenous ECMO in the medical ICU (MICU) at Duke University Medical Center between January 1, 2013, and December 31, 2019. All adult patients (age 18 and over) diagnosed with ARDS and admitted to the MICU within 48 hours of ECMO initiation were included in the analysis. Patients placed on venovenous ECMO for indications other than ARDS were excluded, as were patients placed on ECMO greater than 48 hours prior to admission at our hospital. The primary chart reviewer determined the indication for venovenous ECMO.

Patients were assigned to two study cohorts based on their date of ECMO initiation, with patients placed on ECMO before September 1, 2016 (the date of protocol implementation) in the “before protocol” group, and patients placed on ECMO after that time in the “protocol” group.

Data collected included basic demographics, height and weight at time of cannulation for calculation of body mass index, variables for calculation of Sequential Organ Failure Assessment (SOFA) (15), Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score (16), arterial blood gas values, and Fio2 immediately prior to ECMO cannulation. The dates of hospital admission, initiation of mechanical ventilation, liberation from mechanical ventilation, ECMO cannulation, ECMO decannulation, ICU discharge, and hospital discharge were also recorded for each patient when applicable. The primary chart reviewer determined the first date each patient met criteria for an SOT and the date the first SOT was performed. The total number of SOTs each patient underwent was also recorded.

Intervention

Before the weaning protocol was developed, patients underwent an SOT at attending physician’s discretion. There was no clear guidance or specific criteria for when to perform an SOT, and it was generally based on a clinical impression of improved chest radiograph, lung compliance, and/or gas exchange. After implementation of the SOT protocol, an RT-ECMO specialist assessed each patient at least once every 24 hours and determined if they met the following objective criteria, which were adopted based on consensus opinion of ECMO providers at our institution: pH greater than 7.30, Pao2 greater than 55 torr, ventilator Fio2 less than or equal to 0.40, and tidal volumes greater than or equal to 4 cc/kg of ideal body weight. If the patient met these criteria and were otherwise hemodynamically
stable, the RT-ECMO specialist then independently performed an SOT. ECMO pump settings, including rate of blood flow and sweep gas flow, were not considered as part of the daily readiness assessment.

The SOT was performed by first increasing the Fio₂ on the ventilator to 0.60, and if the patient was not spontaneously breathing, increasing the respiratory rate to meet anticipated minute ventilation demand. Other ventilator settings could be changed per RT-ECMO specialist discretion as long as they adhered to a lung-protective ventilation strategy of tidal volumes less than or equal to 6 cc/kg of ideal body weight, end-inspiratory plateau pressure less than or equal to 30 cm H₂O, and driving pressure less than or equal to 15 cm H₂O. After ventilator adjustment, the sweep gas flow to the ECMO oxygenator was turned off, eliminating ECMO gas exchange. ECMO blood flow was not adjusted.

End-tidal CO₂, pulse oximetry, heart rate, and arterial blood pressure were continuously monitored for acute or detrimental changes for at least 1 hour. Arterial blood gasses were sampled prior to the SOT, every 15 minutes during the first hour of the SOT, and then hourly for the first four hours. If a patient developed worsening respiratory distress or hemodynamic instability, the SOT was immediately terminated, the sweep gas was returned to its previous level, and the ventilator returned to prior settings. The SOT was also terminated if the patient had sustained peripheral oxygen saturation less than 88% or Pao₂ less than 55 torr on Fio₂ of 0.60, or an arterial pH less than 7.30. During the SOT, Fio₂ was weaned as tolerated to target a Pao₂ of 55–80 torr. If the patient maintained adequate gas exchange and hemodynamic stability for 4 hours, they were deemed to have “passed” the SOT. Passage of an SOT, as well as associated vital signs, arterial blood gas results, and ventilator settings, were reported to the attending physician. The ultimate decision to decannulate the patient from venovenous ECMO was left to attending physician discretion (Fig. 1).

**Outcomes**

The primary outcome was duration of venovenous ECMO. Secondary outcomes included duration of mechanical ventilation, ICU LOS, hospital LOS, survival to hospital discharge, and cumulative occurrence rate of ECMO decannulation through 30 days from initiation of ECMO. Time from ECMO initiation to first meeting SOT criteria and first performance of an SOT was calculated for each patient along with time from meeting criteria to decannulation. The total number of SOTs for each patient were also counted. Finally, the number of patients placed back on venovenous ECMO support during the same hospitalization after initial decannulation was recorded.

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**Figure 1.** Daily sweep-off trial (SOT) protocol. Patients were assessed daily with a SOT eligibility screen. If the patient passed the screen and was otherwise hemodynamically stable, then an SOT was performed. If the patient maintained adequate gas exchange and hemodynamic stability for 4 hr, they were deemed to have “passed” the SOT. Patients were considered to “fail” an SOT if they developed worsening respiratory distress or hemodynamic instability, sustained peripheral oxygen saturation less than 88% or Pao₂ less than 55 torr on Fio₂ of 0.60, or an arterial pH less than 7.30. ECMO = extracorporeal membrane oxygenation, IBW = ideal body weight, RR = respiratory rate, Vt = tidal volume.
Statistical Analysis

Demographic and clinical characteristics before and after protocol implementation are presented using the median (25–75th percentiles [Q1–Q3]) for continuous variables or the frequency count and percentage for categorical data. Groups were compared using chi-square or Fisher exact tests for categorical variables and t tests or Wilcoxon rank-sum tests for continuous variables.

Time-varying endpoints were compared using either the Wilcoxon rank-sum test among surviving patients or Fine and Gray’s method accounting for death as a competing risk among all patients, unless otherwise specified. The Gehan-Breslow-Wilcoxon test was used for mechanical ventilation to censor patients discharged on ventilation while putting more weight on early ventilation weaning due to non-proportional hazards (PHs).

Adjusting for baseline SOFA and RESP scores, we applied Cox PHs models with death as a competing risk to compare time to ECMO decannulation, ventilation weaning, ICU discharge, and hospital discharge before and after protocol implementation. In addition, we used standard Cox PH regression methods to evaluate mortality. Results are presented using the hazard ratio (HR) with 95% CI. Among patients surviving to discharge, we implemented an adjusted analysis using negative binomial regression to model ECMO duration, ICU LOS, and hospital LOS with results presented as occurrence rate ratio (IRR) with 95% CI. A Cox PH regression model was used for mechanical ventilation to censor patients not weaned from the ventilator at the time of discharge. If individuals were missing SOFA (n = 3) or RESP (n = 6) scores, the overall median was imputed to avoid excluding subjects in the adjusted models.

All analyses were performed with SAS Version 9.4 (SAS Institute, Cary, NC), and a p value of less than 0.05 was considered statistically significant.

RESULTS

Patient Population and Baseline Characteristics

In total, 245 patients were treated with venovenous ECMO in the MICU at our institution during the study period. Of these patients, 57 were excluded because their indication for venovenous ECMO was not ARDS: 31 bridge to lung transplantation, 10 status asthmaticus, eight lung transplant rejection, four diffuse alveolar hemorrhage, and four for other indications. Eight additional patients were excluded because they were placed on venovenous ECMO greater than 48 hours prior to admission at our hospital. The remaining 180 patients were included in the study analyses.

Of the 180 patients with ARDS managed with venovenous ECMO in the MICU at our institution between January 1, 2013, and December 31, 2019, 67 (37.2%) were managed before implementation of the ECMO weaning protocol, and 113 (62.8%) after implementation. There were no statistically significant differences in baseline severity of illness scores between patients managed on ECMO before and after protocol implementation; however, some differences in baseline characteristics were noted in sex (61.2% male vs 45.1% male; p = 0.037), arterial blood pH (7.25 [7.16–7.33] vs 7.18 [7.09–7.27]; p = 0.003), Paco2 (55 [45–73] vs 61 [51–77]; p = 0.047), and primary diagnosis (46.3% viral pneumonia vs 28.3% viral pneumonia; p = 0.025), respectively (Table 1).

Effect of Protocol Implementation on Timing and Frequency of Sweep-Off Trial

There were no differences before and after protocol implementation in median time from ECMO cannulation to meeting criteria for an SOT (3.0 d [1.0–5.0 d] vs 2.0 d [1.0–3.0 d]; p = 0.089). The cumulative occurrence rate of meeting SOT criteria by day 3 after ECMO cannulation did not differ before and after protocol implementation (56.7% vs 69.9%; p = 0.214).

After protocol implementation, the cumulative occurrence rate of undergoing an SOT among all patients by day 3 was greater (54.9% vs 13.4%; p < 0.001), the time to first SOT performed was shorter (2.5 d [1.0–5.0 d] vs 7.0 d [5.0–11.0 d]; p < 0.001), and the number of SOTs performed per patient was greater (2.0 [1.0–3.0] vs 1.0 [0.0–2.0]; p < 0.001) (Table 2).

Primary Outcome

After implementation of the SOT protocol, the median duration of venovenous ECMO was shorter (5.5 d [3.0–11.0 d] vs 11.0 d [7.0–15.5 d]; p < 0.001) (Table 2). Adjusting for baseline SOFA and RESP scores, after protocol implementation the HR for ECMO decannulation was higher (HR, 1.49; 95% CI, 1.09–2.02; p = 0.011), and patients surviving to discharge were decannulated from ECMO sooner (IRR, 0.65; 95% CI, 0.49–0.86; p = 0.003) (Table 3 and Fig. 2). Finally,
the time from meeting SOT criteria to decannulation among survivors was also shorter after implementation of the SOT protocol (3.0 d [1.0–6.3 d] vs 8.5 d [5.8–13.0 d]; \( p = 0.006 \)).

Secondary Outcomes
After protocol implementation, patients who were liberated from mechanical ventilation had a shorter overall median duration of mechanical ventilation.

### TABLE 1. Baseline Characteristics of Patients Before and After Sweep-Off Trial Protocol Implementation

| Baseline Characteristic                        | Total \((n = 180)\) | Before Protocol \((n = 67)\) | Protocol \((n = 113)\) | \(p\) | Missing, \(n (\%)\) |
|-----------------------------------------------|---------------------|----------------------------|------------------------|------|------------------|
| Age, yr                                       |                     |                            |                        |      |                  |
| Median (25–75th)                              | 44 (33.1–54.0)      | 46 (34.3–59.0)             | 43 (33.0–52.9)         | 0.051| 0 (0.0)          |
| Sex, \(n (\%)\)                               |                     |                            |                        |      |                  |
| Male                                          | 92 (51.1)           | 41 (61.2)                  | 51 (45.1)              | 0.037| 0 (0.0)          |
| Female                                        | 88 (48.9)           | 26 (38.8)                  | 62 (54.9)              |      |                  |
| Race, \(n (\%)\)                              |                     |                            |                        |      |                  |
| White                                         | 112 (64.0)          | 42 (63.6)                  | 70 (64.2)              | 0.114| 5 (2.8)          |
| Black or African American                     | 49 (28.0)           | 22 (33.3)                  | 27 (24.8)              |      |                  |
| Other non-missing                             | 14 (8.0)            | 2 (3.0)                    | 12 (11.0)              |      |                  |
| Body mass index                               |                     |                            |                        | 0.496| 1 (0.6)          |
| Median (25–75th)                              | 32 (25.4–39.5)      | 32 (26.2–38.9)             | 31 (25.4–40.0)         |      |                  |
| Immunocompromised, \(n (\%)\)                |                     |                            |                        | 0.397| 2 (1.1)          |
| No                                            | 143 (80.3)          | 56 (83.6)                  | 87 (78.4)              |      |                  |
| Yes                                           | 35 (19.7)           | 11 (16.4)                  | 24 (21.6)              |      |                  |
| Sequential Organ Failure Assessment score     |                     |                            |                        | 0.711| 3 (1.7)          |
| Median (25–75th)                              | 10 (8.0–13.0)       | 10 (7.0–13.0)              | 10 (8.0–13.0)          |      |                  |
| Respiratory ECMO Survival Prediction score    |                     |                            |                        | 0.186| 6 (3.3)          |
| Median (25–75th)                              | 3 (0.0–5.0)         | 3 (0.0–5.0)                | 3 (0.5–5.0)            |      |                  |
| Arterial blood pH                             |                     |                            |                        | 0.003| 8 (4.4)          |
| Median (25–75th)                              | 7.20 (7.11–7.29)    | 7.25 (7.16–7.33)           | 7.18 (7.09–7.27)       |      |                  |
| \(Pao_2\)                                     |                     |                            |                        | 0.204| 2 (1.1)          |
| Median (25–75th)                              | 64 (54.0–73.0)      | 62 (52.0–70.0)             | 65 (55.0–76.0)         |      |                  |
| \(Paco_2\)                                    |                     |                            |                        | 0.047| 8 (4.4)          |
| Median (25–75th)                              | 60 (49.0–76.0)      | 55 (45.0–73.0)             | 61 (51.0–77.0)         |      |                  |
| \(Pao_2/FIO_2\)                               |                     |                            |                        | 0.210| 2 (1.1)          |
| Median (25–75th)                              | 67 (55.0–86.0)      | 66 (52.0–82.0)             | 68 (58.0–89.0)         |      |                  |
| Ventilator days prior to ECMO                 |                     |                            |                        | 0.075| 0 (0.0)          |
| Median (25–75th)                              | 2 (1.0–5.0)         | 2 (1.0–6.0)                | 1 (1.0–4.0)            |      |                  |
| Primary diagnosis, \(n (\%)\)                |                     |                            |                        | 0.025| 0 (0.0)          |
| Viral pneumonia                               | 63 (35.0)           | 31 (46.3)                  | 32 (28.3)              |      |                  |
| Bacterial pneumonia                           | 27 (15.0)           | 7 (10.4)                   | 20 (17.7)              |      |                  |
| Aspiration                                    | 37 (20.6)           | 8 (11.9)                   | 29 (25.7)              |      |                  |
| Other                                         | 53 (29.4)           | 21 (31.3)                  | 32 (28.3)              |      |                  |

ECMO = extracorporeal membrane oxygenation.
### TABLE 2.
Clinical Endpoints Before and After Sweep-Off Trial Protocol Implementation

| Clinical Endpoint                                      | Total (n = 180) | Before Protocol (n = 67) | Protocol (n = 113) | p       |
|--------------------------------------------------------|-----------------|--------------------------|-------------------|---------|
| Meeting criteria for sweep-off trial                   |                 |                          |                   |         |
| Cumulative occurrence rate at 3 d, % (95% CI)          | 65.0 (57.7–71.4) | 56.7 (44.1–67.5)         | 69.9 (60.6–77.4)  | 0.214   |
| Met criteria, n (%)                                    | 159 (88.3)      | 58 (86.6)                | 101 (89.4)        | 0.570   |
| If yes, median (25–75th) days to criteria met         | 2.0 (1.0–4.0)   | 3.0 (1.0–5.0)            | 2.0 (1.0–3.0)     | 0.089   |
| Sweep-off trial performance                            |                 |                          |                   |         |
| Cumulative occurrence rate at 3 d, % (95% CI)          | 39.4 (32.3–46.5)| 13.4 (6.6–22.8)          | 54.9 (45.3–63.4)  | < 0.001 |
| Sweep-off trial conducted during hospitalization, n (%)| 145 (80.6)      | 49 (73.1)                | 96 (85.0)         | 0.053   |
| If yes, median (25–75th) days to first trial          | 4.0 (2.0–7.0)   | 7.0 (5.0–11.0)           | 2.5 (1.0–5.0)     | < 0.001 |
| Median (25–75th) number of trials                     | 2.0 (1.0–4.0)   | 1.0 (1.0–3.0)            | 2.0 (1.0–5.0)     | 0.003   |
| ECMO duration                                          |                 |                          |                   |         |
| Decannulated from ECMO before death, n (%)            | 126 (70.0)      | 44 (65.7)                | 82 (72.6)         | 0.329   |
| If yes, median (25–75th) duration days                | 7.0 (4.0–13.0)  | 11.0 (7.0–15.5)          | 5.5 (3.0–11.0)    | < 0.001 |
| Mechanical ventilation duration                        |                 |                          |                   |         |
| Weaned from ventilator before discharge, n (%)         | 109 (60.6)      | 36 (53.7)                | 73 (64.6)         | 0.149   |
| If yes, median (25–75th) duration, d                  | 23.0 (11.0–32.0)| 25.0 (21.0–33.0)         | 15.0 (9.0–31.0)   | 0.017   |
| ICU duration                                            |                 |                          |                   |         |
| Discharged from ICU alive, n (%)                      | 120 (66.7)      | 41 (61.2)                | 79 (69.9)         | 0.230   |
| If yes, median (25–75th) ICU length of stay, d        | 23.5 (14.0–35.5)| 27.0 (21.0–36.0)         | 18.0 (10.0–33.0)  | 0.008   |
| Hospital admission duration                            |                 |                          |                   |         |
| Survival to hospital discharge, n (%)                  | 116 (64.4)      | 40 (59.7)                | 76 (67.3)         | 0.306   |
| If yes, median (25–75th) days to discharge            | 34.5 (20.5–50.5)| 35.0 (27.0–48.5)         | 34.0 (18.0–53.5)  | 0.256   |

ECMO = extracorporeal membrane oxygenation.

ventilation (15.0 d [9.0–31.0 d] vs 25.0 d [21.0–33.0 d]; p = 0.017). Those discharged from the ICU after protocol implementation had a shorter ICU LOS (18.0 d [10.0–33.0 d] vs 27.0 d [21.0–36.0 d]; p = 0.008) (Table 2). In multivariate analysis, the duration of mechanical ventilation and ICU LOS were not different between the two groups when including all individuals. However, among those patients in each group that survived until hospital discharge, the observed decrease in duration of mechanical ventilation and ICU LOS after protocol implementation persisted in an adjusted analysis controlling for baseline SOFA and RESP scores (Table 3). No differences in survival or hospital LOS were noted between groups (Tables 2 and 3).

**DISCUSSION**

This retrospective before and after study in patients with ARDS treated with venovenous ECMO found that the implementation of a protocol-directed, RT-ECMO specialist performed, daily assessment of readiness for an SOT was associated with earlier recognition of readiness to wean from ECMO. Implementation of this protocol was associated with shorter time to first SOT, time from meeting SOT criteria to decannulation, and overall duration of ECMO. Multivariate analysis adjusting for baseline SOFA and RESP scores showed an association between protocol implementation and an increased HR for ECMO decannulation, as well as a shorter ECMO duration among patients.
surviving to discharge. Despite no difference between groups in the time to meeting SOT criteria, those in the after protocol group had a shorter time to first SOT and an increased number of SOTs performed, suggesting a treatment effect associated with protocol implementation.

Previous prospective randomized trials have shown that the use of daily, protocol-directed SBTs (“daily SBTs”) and SATs (“daily SATs”) improve outcomes in mechanically ventilated patients when compared with usual care. Importantly, in the trials demonstrating the benefit of daily SBTs and SATs, both the daily assessment of the patient and the performance of the SBT and/or SAT were done by qualified ancillary healthcare staff, including RTs and nurses, and not by the treating physician (9, 12, 14). Our institution developed a protocol for weaning patients with ARDS from venovenous ECMO that built directly on these principles, including a daily assessment of patient readiness to wean, and a trial off ECMO support performed independently by trained RT-ECMO specialists.

Our study has several strengths. This is the first study to attempt to assess the impact of a protocol-directed venovenous ECMO weaning strategy on patient-centered outcomes in those with ARDS treated with venovenous ECMO. Grant et al (5) previously published a daily venovenous ECMO weaning protocol, but this differs significantly from our protocol, as they focused first on decreasing ventilator Fio2 and ECMO pump flow 24–48 hours before weaning sweep gas. Our study is also the first description of a venovenous ECMO weaning protocol that is performed entirely by RT-ECMO specialists or any other nonphysician staff.

Our study has several limitations. There are statistically significant differences in baseline characteristics between groups that could have influenced reported outcomes. The after protocol group had a higher percentage of patients with aspiration pneumonitis as the etiology of respiratory failure, and this has previously been associated with increased survival for patients treated with ECMO (16). However, the SOT group also had a higher Paco2 and lower pH prior to initiation of ECMO, which may indicate a higher dead-space fraction in these patients and has been associated with decreased overall

### TABLE 3. Multivariable Analyses

| Clinical Endpoint                  | HR With 95% CI     | p     |
|-----------------------------------|--------------------|-------|
| ECMO decannulation                | 1.49 (1.09–2.02)   | 0.011 |
| Ventilator liberation             | 1.42 (0.98–2.06)   | 0.065 |
| ICU discharge                     | 1.30 (0.97–1.94)   | 0.075 |
| Hospital discharge                | 1.18 (0.82–1.69)   | 0.379 |
| Mortality                         | 0.79 (0.48–1.31)   | 0.357 |

Survivors After vs Before Protocol Implementation (n = 116)

| Occurrence Rate Ratio With 95% CI | p     |
|-----------------------------------|-------|
| ECMO duration                     | 0.65 (0.49–0.86) | 0.003 |
| ICU length of stay                | 0.77 (0.61–0.98)  | 0.037 |
| Hospital length of stay           | 0.93 (0.73–1.18)  | 0.540 |
| Ventilator liberation             | 2.94 (1.44–6.00)  | 0.003 |

ECMO = extracorporeal membrane oxygenation, HR = hazard ratio.

*Cox proportional hazards used to allow censoring at time of discharge for patients who were discharged still requiring ventilation (n = 10).

All models control for baseline Sequential Organ Failure Assessment (SOFA) and Respiratory ECMO Survival Prediction (RESP) scores. For those missing SOFA (n = 3) or RESP (n = 6) scores, the median was imputed to avoid excluding patients. HR compares time to event, while occurrence rate ratio compares the event duration.

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**Figure 2.** Kaplan-Meier plot of the cumulative occurrence rate of liberation from extracorporeal membrane oxygenation (ECMO) through 30 d of ECMO support. The before protocol group represents patients managed prior to the implementation of the sweep-off trial protocol, and the after protocol group represents patients managed using the sweep-off trial protocol.
odds of survival (17). Notably, the baseline RESP score did not differ significantly between the before and after protocol groups, and multivariable analysis controlling for baseline RESP scores still showed a shortened duration of ECMO in the SOT protocol group. Sex, which also differed significantly between groups, has not been reported to affect outcomes for patients with acute respiratory failure managed with ECMO (16, 18).

Another major limitation of our study is its before-after design, which lends itself to confounding from other temporal trends. It is possible that over the course of the study period changes in the management of patients with ARDS, as well as changes in the management of patients placed on ECMO, could have led to improved outcomes not related to SOT protocol implementation, and are not controlled for in our analysis. In addition, because of the study design, the two groups were not randomized, so other unmeasured confounders not captured by baseline SOFA and RESP score adjustment could also have affected outcomes.

Since the decision to decannulate a patient from ECMO was not protocol-directed in our study, other factors could have played a role in that decision, including input from other specialists, patient trajectory, ECMO complications, and level of ventilatory support. These limitations could be addressed with a future randomized, controlled trial.

The study is retrospective, and as such, adverse events related to SOT performance could not be reliably captured, although in our institutional experience they are rare. Safety of this approach was recently noted in a safety and feasibility trial of a similar daily assessment tool (19). Also, it is important to note that 3.7% patients (3/82) in the after protocol group were placed back on venovenous ECMO support after failing initial decannulation compared with 0% patients (0/44) in the before protocol group. While there were more incidents of need for re cannulation after protocol implementation, it is reassuring that this rate is quite low. Finally, this is a single-center study, which may limit its external validity. Further multicenter studies are needed to validate these results more broadly and also to help define when a patient should be decannulated from ECMO after they have passed an SOT.

**CONCLUSIONS**

We evaluated the impact of implementing a daily, RT-ECMO specialist SOT protocol (“daily SOTs”) to assess readiness to wean from venovenous ECMO support. Patients managed after protocol implementation were identified as meeting criteria for an SOT earlier, received an SOT sooner, and had a shorter ECMO duration. While they were also found to have a shorter duration of mechanical ventilation and ICU LOS, these data are retrospective, and given the limitations of the study’s before-after design, these findings should be considered exploratory. Further investigation of the clinical effectiveness of implementation of a protocol-directed, RT-ECMO specialist performed, daily assessment of readiness for SOT with a prospective, randomized controlled trial is warranted.
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