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Early initiation of physical and occupational therapy while on extracorporeal life support improves patients' functional activity

Emily Cerier[1], **Adwaiy Manerikar**[1], **Viswajit Kandula**[1], **Tara Nykiel**[2], **Shelby Lane**[2], **Rebecca Gabaldon**[2], **Takahide Toyoda**[1], **Yuriko Yagi**[1], **Ankit Bharat**[1,3], **Chitaru Kurihara**[1]

[1]Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

[2]Department of Rehabilitation Services, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

[3]Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

Abstract

Purpose: Managing acute respiratory distress syndrome (ARDS) patients on venovenous extracorporeal membrane oxygenation (V-V ECMO), without sedation/ neuromuscular blockade to allow physical and occupational therapy (PT/OT) participation, is untraditional. Here, we investigate the impact of early PT/OT initiation on discharge functional activity for ARDS patients managed on V-V ECMO.

Methods: This is a retrospective review of 67 ARDS patients managed with V-V ECMO at a single academic center from February 2018 to June 2021. Data collected included patient characteristics, days of V-V ECMO support, day of PT/OT initiation, and ambulation distance and Activity Measure for Post-Acute Care (AMPAC) Six-Clicks score on day of discharge.

Results: Patients with >7 days of V-V ECMO support had decreased ambulation and AMPAC scores compared to those with <7 days (70.5 vs. 162.1, $p < 0.01$ and 12.3 vs. 16.4, $p = 0.01$, respectively). PT/OT initiation within 7 days after starting V-V ECMO significantly improved ambulation and AMPAC scores (163.5 vs. 59.5, $p < 0.001$, and 16.6 vs. 11.8, $p < 0.01$, respectively). Additionally, in patients with >7 days of V-V ECMO support, those who began PT/OT within 8 days of V-V ECMO cannulation had significantly improved ambulation and AMPAC scores (151.8 vs. 44.2, $p < 0.01$, and 16.5 vs. 11.0, $p < 0.01$, respectively).

Correspondence: Chitaru Kurihara, Division of Thoracic Surgery, Northwestern University Feinberg School of Medicine, 676 N. Saint Clair St., Suite 650, Chicago, IL 60611, USA. chitaru.kurihara@northwestern.edu.

AUTHOR CONTRIBUTIONS

Chitaru Kurihara contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Emily Cerier, Adwaiy Manerikar, Viswajit Kandula, Tara Nykiel, Shelby Young, Rebecca Gabaldon, Takahide Toyoda and Yuriko Yagi. The first draft of the manuscript was written by Emily Cerier and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

Conclusion: Early PT/OT initiation in severe ARDS patients managed on V-V ECMO is associated with improved patient functional activity on day of discharge. Our study further supports the use of V-V ECMO in treatment of severe ARDS without sedation/neuromuscular blockade and specifically demonstrates PT/OT should be started early following V-V ECMO cannulation.

Keywords

acute respiratory distress syndrome; extracorporeal life support; occupational therapy; physical therapy

1 | INTRODUCTION

The primary treatment of acute respiratory distress syndrome (ARDS) continues to be lung-protective mechanical ventilation (LP-MV) with low tidal volumes.[1] However, in patients with severe ARDS that are continuing to decompensate, with worsening hypoxemia or respiratory acidosis despite LP-MV with prone position and other standard therapies, venovenous extracorporeal membrane oxygenation (V-V ECMO) has emerged as a well-accepted life-sustaining adjunct treatment.[2] Compared to traditional management of severe ARDS with LP-MV, patients managed with V-V ECMO have decreased 60-day mortality.[3] Despite patients being placed on V-V ECMO for management of severe ARDS, patients continue to receive significant levels of sedation and/or neuromuscular blockade to accommodate continued LP-MV, prohibiting them from any meaningful interactions or participation in therapies, potentially leading to long-term physical and mental sequelae.[4,5]

The use of V-V ECMO has become even more relevant with the devastating impact of coronavirus disease 2019 (COVID-19), as a significant proportion of patients with COVID-19, ranging from 6% to 10%, can progress to ARDS and require mechanical ventilation. V-V ECMO has become a great adjunct treatment modality in treating COVID-19-associated ARDS and those patients often required prolonged V-V ECMO support.[6]

Our institution, as well as others, has previously published on the safety and feasibility of the use of V-V ECMO in treatment of severe ARDS without mechanical ventilation otherwise known as “awake V-V ECMO.”[7–9] However, where the balance falls between the risks and benefits of the discontinuation of mechanical ventilation in V-V ECMO patients remains unclear. While awake V-V ECMO allows for decreased sedation and paralysis, the mechanics of the patient spontaneously breathing may cause uncontrolled inspiratory efforts which could potentially worsen lung injury.[10] One of the major benefits of awake V-V ECMO, decreased sedation and paralysis, allows for early mobilization and participation in physical therapy/occupational therapy (PT/OT). This is especially beneficial for patients who may require prolonged V-V ECMO support. Multiple studies have shown that early mobilization and PT/OT while awake on V-V ECMO is safe and feasible; however, studies with comparative objective data are minimal.[11–15] Initial studies have shown PT/OT while on V-V ECMO can improve patients’ functional capacity, muscle strength, and immobility-associated complications.[14–18] Furthermore, in a scoping review by Polastri et al., they

highlighted the importance of rehabilitative interventions in patients on awake ECMO for COVID ARDS to improve their functional outcomes, while also detailing unique challenges faced providing rehabilitative interventions during the pandemic, from demanding work shifts under harsh conditions to frequently changing COVID protocols.[19] The benefits of early PT/OT and ambulation in the intensive care setting, including improvements in patient delirium rates and functional outcomes, on non-ECMO patients are well published and are being increasingly acknowledged among quality improvement projects.[20–24] Our study aims to determine whether early initiation of PT/OT in severe ARDS patients managed on V-V ECMO can improve day of discharge (DOD) functional activity. Furthermore, our study aims to identify ideal timing of PT/OT initiation in this population and factors which may be associated with worse DOD functional activity.

2 | METHODS

2.1 | Study subjects

This study was approved by the Northwestern University Institutional Review Board (STU00207250) and the need for patient consent for data collection was waived. This is a retrospective review of all patients who underwent V-V ECMO as management for severe ARDS at a single academic center from February 2018 to June 2021. There were 147 V-V ECMO patients identified during this time, and 80 patients were excluded as they died before hospital discharge (Figure 1). Data collected included patients' demographics, comorbidities, V-V ECMO complications, days of V-V ECMO support before PT/OT initiation, and ambulation distance and PT/OT Activity Measure for Post-Acute Care (AMPAC) Six-Clicks score on DOD. The AMPAC Six-Clicks score is a validated assessment of patients' activity limitations in acute care settings and can predict discharge destinations.[25,26] The AMPAC Six-Clicks scores and ambulation distances were obtained from the final PT/OT notes prior to discharge from the hospital.

2.2 | Indication of ECMO

Patients with respiratory failure were considered for V-V ECMO if they failed to achieve satisfactory gas exchange (PaO_2 > 55 mmHg, Oxygen saturations >88%, pH >7.2, with plateau pressures less than 35) despite LP-MV and recruitment maneuvers with or without neuromuscular blockade. Our institution has previously reported, in a single-center case series comparing V-V ECMO outcomes between those with COVID-19 ARDS and those without COVID-19, that early initiation (within 7 days of initiation of intubation) of V-V ECMO is important for improved outcomes in COVID-19 ARDS.[6] Therefore, our institution considers greater than 7 days from intubation to be a relative contraindication to V-V ECMO. The decision to cannulate was made by a multidisciplinary ECMO team. All patients were cannulated by thoracic surgeons.

2.3 | V-V ECMO management

Patients did not receive continuous anticoagulation unless there was a specific indication, such as deep venous thrombosis (DVT) or pulmonary embolism (PE), and there was no monitoring of bleeding parameters such as the activated clotting time or activated partial thromboplastin time, consistent with our prior study.[27] All patients who were not receiving

continuous systemic anticoagulation received 5000 U subcutaneous unfractionated heparin every 8 h as a prophylaxis dose to prevent DVT. V-V ECMO flow was maintained at a minimum of 3.0–3.5 L/min, consistent with our recent reports, to reduce thrombotic complications in the ECMO circuit.[27, 28, 7] Transfusions were administered if any of the following criteria were met: platelets <50 000/ml, hemoglobin <7 g/dl, or hemodynamic instability in the setting of active blood loss. Different cannulation strategies (Internal jugular vein—femoral vein cannulation vs. ProtekDuo® cannulation [CardiacAssist Inc., Pittsburgh, PA, USA]) were used in patients depending on surgeon preference. The V-V ECMO circuit included a Quadrox-iD adult (7.0) oxygenator (MAQUET Holding B.V. & Co. KG, Germany) and Rotaflow pump (MAQUET Holding B.V. & Co. KG, Germany). All components of the ECMO circuit had a heparin coating except for the cannulas. Extended V-V ECMO runs were defined as any V-V ECMO run greater than 7 days.

2.4 | PT/OT intervention

The physical and occupation therapists at our institution go through formalized training to be able to conduct PT/OT sessions with V-V ECMO patients. First, the therapists are given a thorough introduction to V-V ECMO, where they learn background information regarding the indications, types/cannulation strategies, and components of the ECMO machine. Additionally, they learn the role of necessary providers (i.e., nurse, ECMO specialist, and respiratory therapist), how to interpret ECMO settings and pertinent laboratory values, potential ECMO complications (i.e., chugging, low flow, and cannulation site integrity) and management/safe practices of cannulation sites. Following, therapists review our standardized protocols for PT/OT in V-V ECMO patients, which review criteria for mobility, considerations for therapy, and implement therapeutic interventions safely and effectively. Then, therapists will shadow already trained therapists during sessions, where they gain hands-on experience in working with V-V ECMO patients, performing verticalization, dangling, standing, ambulating, activities of daily living, dynamic balance, and high level strength and aerobic conditioning exercises. After shadowing, therapists must review a PT/OT V-V ECMO clinical competency before they are able to officially work with V-V ECMO patients.

Patients begin PT/OT while on V-V ECMO if deemed medically appropriate by a multidisciplinary team. Possible contraindications to PT/OT include sedation prohibiting participation in meaningful activity and neuromuscular blockade. Relative considerations to PT/OT warranting further assessment of the patient condition include unstable cannulation, unstable V-V ECMO flows, excessive recirculation, open chest/abdomen, femoral arterial sheaths, active bleeding, and number and dosing of vasoactive drips. If any contraindications are identified or the multidisciplinary team deems the patient unsafe, PT/OT initiation is delayed. All PT/OT sessions include the presence of the nurse, ECMO specialist, physical or occupational therapist, and respiratory therapist if the patient requires high flow oxygen or mechanical ventilation, and all therapy sessions begin with a formal “time out.” Following, V-V ECMO patients are progressed from verticalization, to dangling at the edge of bed, activities of daily living, standing, ambulating, aerobic training, and stair negotiation based on their exercise tolerance and personalized treatment plans. The physical and occupational therapists collaborate very closely with each other and with the medical teams.[29] On a

patient-by-patient basis, the physical and occupational therapists develop treatment plans for each patient, individualizing the intensity and frequency of therapy sessions. These procedures are similar to previously published V-V ECMO PT/OT procedures and consensus guidelines.[12,13]

In our study, early PT/OT initiation was defined as therapy that started within 7 days from V-V ECMO cannulation. Previous randomized controlled clinical trial, patients were randomized to either early mobilization or standard of care mobilization within 72 hours of ECMO initiation. They reported that the standard of care group began PT/OT on study day 4 from randomization, which would roughly be day 7 from ECMO commencement.[30]

2.5 | Definition of complication

Post-cannulation complications were determined using the following definitions:

- *Gastrointestinal bleeding* was defined as one or more of the following: guaiac-positive stool, hematemesis melena, active bleeding at the time of endoscopy or colonoscopy, or blood within the stomach at endoscopy or colonoscopy.
- *Hemothorax* was defined as the presence of blood in the chest cavity, typically confirmed via chest x-ray or computed tomography (CT) scan. Hemothorax occurring as a result of surgery was exempt from this definition.
- *Diffuse alveolar hemorrhage* was defined as hemorrhage in the alveoli, confirmed via bronchoscopy.
- *DVT and PE* were determined by duplex ultrasonography and pulmonary CT angiograms, respectively.
- *Ischemic fingers* were determined by vascular surgeons with clinical symptoms.
- *Sepsis* was defined as bacteremia confirmed via blood cultures.
- *Neurological dysfunction* was a new neurological deficit associated with abnormal neuroimaging findings. This was further divided into ischemic or hemorrhagic based on imaging findings.
- *Acute kidney injury (AKI)* was defined using the Risk, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) classification.[31]

For the purposes of this study, only complications occurring while the patient was still undergoing V-V ECMO support were considered. Complications occurring after decannulation were not included.

2.6 | Statistical analysis

Patient demographics, post-ECMO complications, and functional outcomes were compared between those patients with ECMO support less than 7 days and over 7 days as well as those with PT/OT initiation within 7 days and over 7 days of V-V ECMO cannulation. An additional sub-group analysis was performed in the cohort of patients with ECMO support for over 7 days, comparing those with PT/OT initiation within 8 days and over 8 days from cannulation. Continuous variables were compared using Student's *t*-test and reported

as means. Categorical variables were compared using chi-square test and reported as a number (percentage). *p*-values <0.05 were accepted as statistically significant. We used EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Patient demographics and overall outcomes

There were 67 patients that met inclusion criteria for this study, of which 32 (47.7%) patients were placed on V-V ECMO due to COVID ARDS (Figure 1). The mean age and body mass index of patients was 46.2 years and 31.6 kg/m^2, respectively, and 29 (43.3%) patients were female. Common patient comorbidities included hypertension (*n* = 25, 37.7%), diabetes mellitus (*n* = 17, 25.4%), and smoking history (*n* = 17, 25.4%). Patients were intubated for an average of 4 days (standard deviation 4.5 days) prior to V-V ECMO cannulation and 22 (32.8%) patients received lung transplants. The most common V-V ECMO complications encountered were AKI (*n* = 32, 47.8%), sepsis (*n* = 28, 41.8%), thrombotic event (*n* = 24, 35.8%), and bleeding event (*n* = 16, 23.9%).

3.2 | Factors associated with functional capacity on day of discharge

3.2.1 | Short versus extended V-V ECMO runs

Study population: A total of 44 (65.7%) patients had an extended V-V ECMO run (>7 days). There were no significant differences in pre-V-V ECMO cannulation characteristics between patients with short vs. extended V-V ECMO runs, except for pre-V-V ECMO cannulation albumin level (3.2 g/dl vs. 2.8 g/dl, $p = 0.04$, respectively) (Table 1).

Outcomes: Patients undergoing an extended V-V ECMO run were more likely to experience bleeding events and sepsis when compared to patients with a short V-V ECMO run (14 (31.8%) vs. 2 (8.7%), $p = 0.04$ and 24 (54.5%) vs. 4 (17.4%), $p < 0.01$, respectively). Patients with an extended V-V ECMO run were more likely to undergo lung transplantation (19 (43.2%) vs. 3 (13%), $p = 0.01$) (Table 2). Those with >7 days on V-V ECMO had decreased ambulation and AMPAC scores on DOD compared to those with <7 days on V-V ECMO (70.5 ft vs. 162.1 ft, $p < 0.01$, and 12.3 vs. 16.4, $p = 0.01$, respectively).

3.2.2 | Early versus delayed PT and OT initiation

Study population: There were 37 (55.2%) patients who had delayed initiation of PT/OT following V-V ECMO cannulation (>7 days). There were no significant differences in pre-V-V ECMO cannulation characteristics between patients with early vs. delayed PT/OT initiation (Table 3).

Outcomes: Patients with delayed PT/OT initiation were more likely to experience sepsis compared to those with early PT/OT initiation (21 [56.8%] vs. 7 [23.3%], $p = 0.01$); however, there were no other major differences in V-V ECMO complications between patients with delayed vs. early PT/OT initiation. Patients with delayed PT/OT initiation were more likely to undergo lung transplant (17 [45.9%] vs. 5 [16.7%], $p = 0.02$) (Table 4). Early PT/ OT initiation after starting V-V ECMO significantly improved ambulation distance and

AMPAC scores on DOD compared to those with delayed PT/OT initiation (163.5 ft vs. 59.5 ft, $p < 0.001$ and 16.6 vs. 11.8, $p < 0.01$, respectively).

3.2.3 | Early versus delayed PT and OT initiation in extended V-V ECMO runs

Study population: In those patients with extended V-V ECMO runs ($n = 44$), 31 (70.5%) patients had >8 days following V-V ECMO cannulation prior to PT/OT initiation. There were no significant differences in pre-V-V ECMO cannulation characteristics between the extended V-V ECMO run patients who had early (<8 days from V-V ECMO cannulation) vs. delayed (>8 days following V-V ECMO cannulation) PT/OT initiation (Table 5).

Outcomes: There were no significant differences in V-V ECMO complications between extended V-V ECMO run patients with delayed vs. early PT/OT initiation (Table 6). In extended V-V ECMO support patients, those with early PT/OT initiation had improved ambulation distances and AMPAC scores on DOD compared to those with delayed PT/OT initiation (151.8 ft vs. 44.2 ft, $p < 0.01$, and 16.5 vs. 11.0, $p < 0.01$, respectively).

4 | DISCUSSION

Multiple studies have been published on the safety, feasibility, and benefits of PT/OT while patients are on V-V ECMO.[11–18] Our study goes beyond the safety, feasibility, and benefits of PT/OT while on V-V ECMO, and reports objective data showing clear benefits of, specifically, early initiation of PT/OT in V-V ECMO patients. Early initiation of PT/OT in V-V ECMO patients is critical to improve patients' functional outcomes, especially in those expected to have long V-V ECMO runs.[32] This is particularly pertinent to the current COVID-19 pandemic, as patients with COVID-19-associated ARDS who require V-V ECMO tend to have prolonged support days. Our institution has reported, in a single-center case series describing the clinical characteristics and outcomes of lung transplant patients who had COVID-19-associated ARDS, that COVID-19-associated ARDS V-V ECMO patients should be supported for at least 4 weeks before consideration of lung transplantation. Therefore, V-V ECMO support days tend to be prolonged in these patients and our institution only considers lung transplantation in ARDS V-V ECMO patients who have had greater than 28 days of V-V ECMO support.[33,34] With increasing duration of V-V ECMO runs being utilized as bridge to lung transplant across the country, improving patients' functional outcomes should be prioritized as patients requiring V-V ECMO before or after lung transplantation tend to have worse physical function at ICU and hospital discharge compared to those that did not require V-V ECMO.

4.1 | Early PT/OT initiation improves patients' functional outcomes

Initial studies have shown PT/OT while on V-V ECMO can improve patients' functional capacity, muscle strength, and immobility-associated complications, even in patients with COVID-19.[14–19] However, these studies do not specifically analyze the impact of timing of PT/OT initiation on patient functional outcomes by directly comparing patients with early PT/OT initiation to those with delayed PT/OT initiation. To the best of our knowledge, our study is the first to show that early initiation of PT/OT in V-V ECMO patients, as defined as within 7 days of V-V ECMO cannulation, is associated with significantly improved

ambulation and AMPAC scores on DOD. Patients with initiation of PT/OT within 7 days of starting V-V ECMO were able to ambulate on DOD an average of 104 ft farther than patients with greater than 7 days of V-V ECMO prior to PT/OT initiation. Furthermore, those patients with early initiation of PT/OT had AMPAC scores on DOD 4.8 points higher than those with delayed PT/OT initiation. Those patients with early compared to delayed PT/OT initiation had no significant differences in pre-V-V ECMO cannulation characteristics, therefore minimizing any baseline characteristic confounding variables. However, those patients with delayed PT/OT initiation were more likely to experience sepsis and undergo V-V ECMO as a bridge to lung transplantation. This could raise the concern that those patients in the delayed cohort were more critically ill leading to delayed PT/OT and had more complicated hospital courses, potentially affecting their functional outcome on DOD. Regardless, the cohort of V-V ECMO patients with early PT/OT initiation had no significantly higher rates of V-V ECMO complications (Table 4). This shows that specifically, early PT/OT initiation, defined as within 7 days of V-V ECMO cannulation, is safe and feasible in V-V ECMO patients.

Our study demonstrates that the first week of V-V ECMO is a critical time period for which patients' functional outcomes may be impacted by the initiation of PT/OT. Therefore, this study provides support for the implementation and development of V-V ECMO protocols to optimize patients to be able to participate in early PT/OT, including practices such as minimizing sedation, early extubation, avoiding femoral arterial lines, etc.[7] While V-V ECMO PT/OT protocols may be costly, due to increased staffing needs and training, formalized cost–benefit analyses are needed to determine their exact impact as the benefits expand beyond patients' functional outcomes. For example, improving patients' ambulation on day of discharge not only has the possibility to improve patients' overall functional outcomes, but also their 30-day readmission rates as Jeong et al found that post-cardiac surgery patients' ambulation profiles were predictive of 30-day readmission.[35]

4.2 | Extended V-V ECMO runs are associated with decreased functional capacity on day of discharge and early PT/OT Initiation In Extended V-V ECMO runs allows recovery of functional capacity

Prolonged V-V ECMO runs are associated with lower survival rates when compared to short V-V ECMO runs.[36] However, not only are extended V-V ECMO runs associated with lower survival rates, but also worse patient functional outcomes. Our study demonstrated that patients with extended V-V ECMO runs had two times shorter ambulation distances on DOD when compared to patients with short V-V ECMO runs. Additionally, our study showed AMPAC scores on DOD for patients with extended V-V ECMO runs were 4.1 points less than those patients with short V-V ECMO runs. However, when looking at pre-V-V ECMO cannulation characteristics, those patients with extended V-V ECMO runs were more likely to have lower albumin levels, which could serve as a marker for worse nutritional status and be a confounder in this analysis. Furthermore, those patients with extended V-V ECMO runs were also more likely to have V-V ECMO complications and undergo lung transplant, which could be indicative of more complex hospital courses, prohibiting PT/OT initiation, and further confound this analysis. Regardless, as V-V ECMO is becoming more common, and runs are becoming longer, these results highlight the importance of

optimizing the management of those patients on extended V-V ECMO runs to improve patient outcomes.

While our study showed extended V-V ECMO runs are associated with worse functional capacity on DOD, our study also found that this functional capacity could be recovered by early initiation of PT/OT in this cohort. In patients with extended V-V ECMO runs, our study found when PT/OT was initiated within 8 days of V-V ECMO cannulation, patients had improved functional outcomes. Extended V-V ECMO run patients with early PT/OT initiation (defined as within 8 days of cannulation) were able to ambulate nearly 3.5 times farther than those extended V-V ECMO run patients with delayed PT/OT initiation. Additionally, extended V-V ECMO run patients with early PT/OT initiation had AMPAC scores on DOD 4.5 points higher than those with delayed PT/OT initiation. Extended V-V ECMO run patients with early PT/OT initiation had ambulation distances and AMPAC scores on DOD which rivaled those with short V-V ECMO runs (151.8 ft vs. 162.1 ft, and 16.5 vs. 16.4, respectively). This suggests that early initiation of PT/OT in extended V-V ECMO runs can recover functional capacity that can be lost due to extended V-V ECMO runs. Additionally, when analyzing extended V-V ECMO run patients with early vs. delayed PT/OT initiation, there were no significant differences in their pre-V-V ECMO cannulation characteristics, V-V ECMO complications, or lung transplantation rate, therefore minimizing any confounding variables.

4.3 | Limitations and further studies

While this study shows clear support for early PT/OT initiation in V-V ECMO patients to improve functional outcomes, it is not without limitations. First, this study was a single institution, retrospective observational study and therefore our results may not be generalizable to other V-V ECMO institutions and we are limited by misclassification bias. Second, given the smaller sample sizes of our study, it is difficult to adjust for potential cofounders as noted previously for certain subgroups. Additionally, this study does not address any impact early PT/OT initiation following V-V ECMO cannulation may have on patients' survival rates. Further multi-institutional, prospective studies using standardized protocols are needed to better clarify the impact of early PT/OT initiation in V-V ECMO patients. Additionally, studies are needed to analyze the cost–benefit analyses of implementing protocols for early PT/OT initiation in V-V ECMO patients.

5 | CONCLUSION

Extended V-V ECMO runs in severe ARDS patients are associated with decreased patient functional capacity on DOD. Conversely, early PT/OT initiation in severe ARDS patients managed on V-V ECMO is associated with improved patient functional activity on DOD. For those severe ARDS patients managed with extended V-V ECMO runs, early PT/OT initiation is of critical importance to recover patients' functional outcomes. Therefore, our study further supports the use of V-V ECMO in treatment of severe ARDS without mechanical ventilation, sedation or neuromuscular blockade to allow for early initiation of PT/OT to improve patients' functional capacity on DOD. Improved functional activity

on DOD may provide benefits such as enhanced recovery, increased ability to complete activities of daily living, and improved cognitive health.

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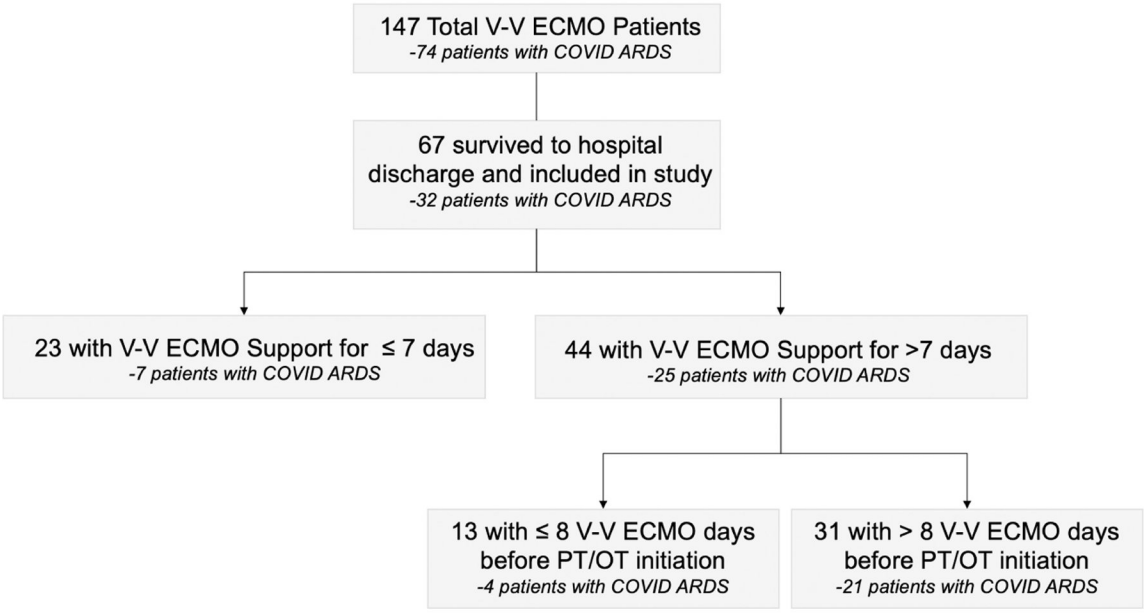

FIGURE 1.

Flow diagram of patient selection. There were 147 total V-V ECMO patients at our institution from February 2018 to June 2021. 67 patients then survived to hospital discharge and were subsequently included in this study. Additionally, number of patients with COVID ARDS in each sub-group is also indicated.

TABLE 1

Characteristics of patients by V-V ECMO support duration

Variable	Overall (*n* = 67)	V-V ECMO ≤7 days (*n* = 23)	V-V ECMO >7 days (*n* = 44)	*p* value
Age, years	46.2 ± 13.7	46.7 ± 16.7	46 ± 12	0.86
Female	29 (43.3%)	10 (43.5%)	19 (43.2%)	1.00
BMI, kg/m^2	31.6 ± 9	32.9 ± 9.3	30.9 ± 8.9	0.39
BSA, m^2	2.1 ± 0.3	2.1 ± 0.3	2 ± 0.3	0.44
Smoking history	17 (25.4%)	8 (34.8%)	9 (20.5%)	0.24
Hypertension	25 (37.3%)	8 (34.8%)	17 (38.6%)	0.80
Diabetes mellitus	17 (25.4%)	4 (17.4%)	13 (29.5%)	0.38
CKD	8 (11.9%)	3 (13%)	5 (11.4%)	1.00
Dialysis	7 (10.4%)	1 (4.3%)	6 (13.6%)	0.41
Laboratory				
Hemoglobin, g/dl	11.5 ± 2.3	11.8 ± 2.6	11.3 ± 2.1	0.44
WBC, 1000/mm^3	13.1 ± 6.7	12.3 ± 6.7	13.6 ± 6.8	0.49
Platelets, 1000/mm^3	244.6 ± 116.1	233.1 ± 79.2	252.3 ± 135.9	0.51
Sodium, mEq/L	139.2 ± 5.4	138.7 ± 4.5	139.5 ± 5.9	0.57
Creatinine, mg/dl	1 ± 0.7	1.2 ± 0.9	0.9 ±0.5	0.10
BUN, mg/dl	21.9 ± 13.4	23.9 ± 17.7	20.6 ± 9.5	0.43
AST, U/L	65 ± 83.5	63 ± 87.1	66.3 ± 82.7	0.90
ALT, U/L	61.6 ± 70.8	50.2 ± 54.1	68.6 ± 79.3	0.33
Total bilirubin, mg/dl	0.8 ± 0.7	0.9 ± 0.7	0.8 ± 0.7	0.84
Albumin, g/dl	2.9 ±0.6	3.2 ±0.8	2.8 ± 0.5	0.04
INR	1.2 ± 0.2	1.1 ± 0.1	1.2 ±0.3	0.06
ABG (at cannulation)				
pH	7.3 ± 0.1	7.27 ± 0.1	7.31 ± 0.1	0.11
PaCO2	57.1 ± 16.3	57.1 ± 15.1	57.2 ± 17.3	0.98
PaO_2	94.2 ± 63.1	97.7 ± 81.2	91.7 ± 47.5	0.76
HCO_3	28.3 ± 7.5	26.3 ± 6.8	29.7 ± 7.8	0.10
Lactate	2.7 ±2.5	3.1 ± 2.7	2.5 ± 2.4	0.43
Days from Intubation to V-V ECMO cannulation	4.1 ± 4.5	3 ± 3.1	4.7 ± 5	0.14

Note: Continuous data are shown as means ± standard deviation (SD).

Abbreviations: ABG, arterial blood gas; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BSA, body surface area; BUN, blood urea nitrogen; CKD, chronic kidney disease; INR, international normalized ratio; WBC, white blood cell.

TABLE 2

Outcomes of patients by V-V ECMO support duration

Variable	Overall (*n* = 67)	V-V ECMO ≤7 days (*n* = 23)	V-V ECMO >7 days (*n* = 44)	*p* value
Day of discharge AMPAC score	14 ± 6.6	16.4 ± 6.8	12.3 ± 5.9	0.010
Day of discharge ambulation distance	106.1 ± 137.1 ft	162.1 ± 154.1 ft	70.5 ± 113.3 ft	<0.01
Lung transplant	22 (32.8%)	3[a] (13%)	19 (43.2%)	0.01
Pneumothorax	21 (31.3%)	4 (17.4%)	17 (38.6%)	0.09
Total bleeding events	16 (23.9%)	2 (8.7%)	14 (31.8%)	0.04
Hemothorax	8 (11.9%)	3 (13%)	5 (11.4%)	1.00
Tracheostomy bleeding	7 (10.4%)	0 (0%)	7 (15.9%)	0.09
Cannulation bleeding	2 (3%)	1 (4.3%)	1 (2.3%)	1.00
GI bleeding	1 (1.5%)	0 (0%)	1 (2.3%)	1.00
Neurologic dysfunction	1 (1.5%)	0 (0%)	1 (2.3%)	1.00
Ischemic stroke	1 (1.5%)	0 (0%)	1 (2.3%)	1.00
Hemorrhage stroke	2 (3%)	0 (0%)	2 (4.5%)	0.54
Total thrombotic events	24 (35.8%)	7 (30.4%)	17 (38.6%)	0.60
DVT	19 (28.4%)	3 (13%)	16 (36.4%)	0.05
PE	4 (6%)	2 (8.7%)	2 (4.5%)	0.60
Ischemic digits	5 (7.5%)	1 (4.3%)	4 (9.1%)	0.65
Ischemic bowel	2 (3%)	1 (4.3%)	1 (2.3%)	1.00
AKI	32 (47.8%)	8 (34.8%)	24 (54.5%)	0.19
Dialysis	18 (26.9%)	4 (17.4%)	14 (31.8%)	0.26
Sepsis	28 (41.8%)	4 (17.4%)	24 (54.5%)	<0.01

Note: Continuous data are shown as means ± standard deviation (SD).

Abbreviations: AKI, acute kidney injury; AMPAC, Activity Measure for Post-Acute Care; DVT, deep vein thrombosis; GI, gastrointestinal; PE, pulmonary embolism.

[a]These patients were on V-V ECMO following lung transplant.

TABLE 3

Characteristics of patients by timing of PT/OT initiation

Variable	Overall (*n* = 67)	≤7 V-V ECMO days before OT/PT (*n* = 30)	>7 V-V ECMO Days Before OT/PT (*n* = 37)	*p* value
Age, years	46.2 ± 13.7	46.7 ± 15.7	45.9 ± 12	0.82
Female	29 (43.3%)	11 (36.7%)	18 (48.6%)	0.46
BMI, kg/m^2	31.6 ± 9	32.1 ± 9.1	31.2 ± 9.1	0.69
BSA, m^2	2.1 ± 0.3	2.1 ± 0.3	2 ± 0.3	0.41
Smoking history	17 (25.4%)	10 (33.3%)	7 (18.9%)	0.26
Hypertension	26 (38.8%)	11 (36.7%)	15 (40.5%)	0.80
Diabetes mellitus	17 (25.4%)	7 (23.3%)	10 (27%)	0.78
CKD	8 (11.9%)	4 (13.3%)	4 (10.8%)	1.00
Dialysis	7 (10.4%)	2 (6.7%)	5 (13.5%)	0.45
Laboratory				
Hemoglobin, g/dl	11.5 ± 2.3	11.9 ± 2.3	11 ± 2.3	0.17
WBC, 1000/mm^3	13.1 ± 6.7	12.2 ± 6.5	14.1 ± 6.9	0.32
Platelets, 1000/mm^3	244.6 ± 116.1	243.3 ± 131.7	246.1 ± 98.4	0.93
Sodium, mEq/L	139.2 ± 5.4	137.8 ± 5.1	140.7 ± 5.4	0.05
Creatinine, mg/dl	1 ± 0.7	1.1 ±0.8	0.9 ± 0.5	0.28
BUN, mg/dl	21.9 ± 13.4	22.6 ± 16.1	21.2 ± 9.7	0.70
AST, U/L	65 ± 83.5	62.3 ± 77	68 ± 91.6	0.81
ALT, U/L	61.6 ± 70.8	60.1 ± 53.9	63.3 ± 86.7	0.88
Total bilirubin, mg/dl	0.8 ± 0.7	0.9 ± 0.7	0.8 ± 0.7	0.93
Albumin, g/dl	2.9 ±0.6	3 ± 0.6	2.8 ± 0.6	0.21
INR	1.2 ± 0.2	1.2 ± 0.1	1.2 ± 0.3	0.28
ABG (at cannulation)				
pH	7.3 ± 0.1	7.28 ± 0.1	7.31 ± 0.1	0.29
PaCO2	57.1 ± 16.3	56.1 ± 14.7	58.4 ± 18.2	0.62
PaO_2	94.2 ± 63.1	85 ± 44.2	104.5 ± 78.8	0.28
HCO3	28.3 ± 7.5	26.6 ± 6.6	30.3 ± 8.1	0.08
Lactate	2.7 ±2.5	2.7 ± 2.4	2.7 ± 2.7	0.95
Days from Intubation to V-V ECMO cannulation	4.1 ± 4.5	3.5 ± 4.4	4 ± 4.6	0.65

Note: Continuous data are shown as means ± standard deviation (SD).

Abbreviations: ALT, Alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BSA, body surface area; BUN, blood urea nitrogen; CKD, chronic kidney disease; INR, international normalized ratio; WBC, white blood cell.

TABLE 4

Outcomes of V-V ECMO patients by timing of PT/OT initiation

Variable	Overall (*n* = 67)	≤7 V-V ECMO days before OT/PT (*n* = 30)	>7 V-V ECMO Days Before OT/PT (*n* = 37)	*p* value
Day of discharge AMPAC score	14 ± 6.6	16.6 ± 7.1	11.8 ± 5.2	<0.01
Day of discharge ambulation distance	106.1 ± 137.1 ft	163.5 ± 160.5 ft	59.5 ± 93.5 ft	<0.001
Lung transplant	22 (32.8%)	5 (16.7%)	17 (45.9%)	0.02
Pneumothorax	21 (31.3%)	9 (30%)	12 (32.4%)	1.00
Total bleeding events	16 (23.9%)	5 (16.7%)	11 (29.7%)	0.26
Hemothorax	8 (11.9%)	4 (13.3%)	4 (10.8%)	1.00
Tracheostomy bleeding	7 (10.4%)	2 (6.7%)	5 (13.5%)	0.45
Cannulation bleeding	2 (3%)	1 (3.3%)	1 (2.7%)	1.00
GI bleeding	1 (1.5%)	0 (0%)	1 (2.7%)	1.00
Neurologic dysfunction	1 (1.5%)	0 (0%)	1 (2.8%)	1.00
Ischemic stroke	1 (1.5%)	0 (0%)	1 (2.7%)	1.00
Hemorrhage stroke	2 (3%)	0 (0%)	2 (5.4%)	0.50
Total thrombotic events	24 (35.8%)	9 (30%)	15 (40.5%)	0.45
DVT	19 (28.4%)	5 (16.7%)	14 (37.8%)	0.06
PE	4 (6%)	2 (6.7%)	2 (5.4%)	1.00
Ischemic digits	5 (7.5%)	1 (3.3%)	4 (10.8%)	0.37
Ischemic bowel	2 (3%)	1 (3.3%)	1 (2.7%)	1.00
AKI	32 (47.8%)	12 (40%)	20 (54.1%)	0.33
Dialysis	18 (26.9%)	6 (20%)	12 (32.4%)	0.28
Sepsis	28 (41.8%)	7 (23.3%)	21 (56.8%)	0.01

Note: Continuous data are shown as means ± standard deviation (SD).

Abbreviations: AKI, acute kidney injury; AMPAC, Activity Measure for Post-Acute Care; DVT, deep vein thrombosis; GI, gastrointestinal; PE, pulmonary embolism.

TABLE 5

Characteristics of patients with over 7 days of V-V ECMO support by timing of PT/OT initiation

Variable	Overall (*n* = 44)	≤8 V-V ECMO days before PT/OT (*n* = 13)	>8 V-V ECMO Days Before PT/OT (*n* = 31)	*p* value
Age, years	46 ± 12	48 ± 10.1	45.2 ± 12.8	0.44
Female	19 (43.2%)	3 (23.1%)	16 (51.6%)	0.10
BMI, kg/m^2	30.9 ± 8.9	29.2 ± 7.1	31.6 ± 9.5	0.37
BSA, m^2	2 ± 0.3	2.1 ± 0.3	2 ± 0.4	0.66
Smoking history	9 (20.5%)	5 (38.5%)	4 (12.9%)	0.10
Hypertension	17 (38.6%)	5 (38.5%)	12 (38.7%)	1.00
Diabetes mellitus	13 (29.5%)	5 (38.5%)	8 (25.8%)	0.48
CKD	5 (11.4%)	3 (23.1%)	2 (6.5%)	0.14
Dialysis	6 (13.6%)	2 (15.4%)	4 (12.9%)	1.00
Laboratory				
Hemoglobin, g/dl	11.3 ± 2.1	11.8 ± 1.8	10.9 ± 2.3	0.26
WBC, 1000/mm^3	13.6 ± 6.8	12.4 ± 4.9	14.4 ± 7.8	0.35
Platelets, 1000/mm^3	252.3 ± 135.9	286.9 ± 184.5	229.8 ± 91	0.31
Sodium, mEq/L	139.5 ± 5.9	138.2 ± 6.3	140.3 ± 5.7	0.35
Creatinine, mg/dl	0.9 ± 0.5	0.9 ± 0.6	0.9 ± 0.4	0.94
BUN, mg/dl	20.6 ± 9.5	19.8 ± 8.7	21.2 ± 10.1	0.70
AST, U/L	66.3 ± 82.7	45.4 ± 36.2	81.4 ± 102.8	0.18
ALT, U/L	68.6 ± 79.3	55.2 ± 48.8	78.3 ± 95.8	0.39
Total bilirubin, mg/dl	0.8 ± 0.7	0.9 ± 1	0.7 ± 0.4	0.50
Albumin, g/dl	2.8 ± 0.5	2.9 ± 0.4	2.7 ± 0.4	0.18
INR	1.2 ± 0.3	1.2 ± 0.1	1.3 ± 0.3	0.20
ABG (at cannulation)				
pH	7.31 ± 0.1	7.33 ± 0.1	7.3 ± 0.1	0.44
PaCO2	57.2 ± 17.3	54.1 ± 12.5	59.2 ± 19.9	0.39
PaO_2	91.7 ± 47.5	109.3 ± 67.3	80.6 ± 25.7	0.18
HCO3	29.7 ± 7.8	30.8 ± 9.1	29.1 ± 7	0.59
Lactate	2.5 ± 2.4	1.7 ± 0.5	2.9 ± 2.9	0.09
Days from intubation to V-V ECMO cannulation	4 ± 4.5	4 ± 4.2	5 ± 4.8	0.52

Note: Continuous data are shown as means ± standard deviation (SD).

Abbreviations: ABG, arterial blood gas; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BSA, body surface area; BUN, blood urea nitrogen; CKD, chronic kidney disease; INR, international normalized ratio; WBC, white blood cell.

TABLE 6

Outcomes of patients with more than 7 days of V-V ECMO support by timing of PT/OT initiation

Variable	Overall (*n* = 44)	≤8 V-V ECMO days before OT/PT (*n* = 13)	>8 V-V ECMO Days Before OT/PT (*n* = 31)	*p* value
Day of discharge AMPAC score	14 ± 6.6	16.5 ± 7.4	11 ± 4.6	<0.01
Day of discharge ambulation distance	106.1 ± 137.1 ft	151.8 ± 160.7 ft	44.2 ± 77.8 ft	<0.01
Lung transplant	19 (43.2%)	4 (30.8%)	15 (48.4%)	0.33
Pneumothorax	17 (38.6%)	6 (46.2%)	11 (35.5%)	0.52
Total bleeding events	14 (31.8%)	3 (23.1%)	11 (35.5%)	0.50
Hemothorax	5 (11.4%)	1 (7.7%)	4 (12.9%)	1.00
Tracheostomy bleeding	7 (15.9%)	3 (23.1%)	4 (12.9%)	0.40
Cannulation bleeding	1 (2.3%)	0 (0%)	1 (3.2%)	1.00
GI bleeding	1 (2.3%)	0 (0%)	1 (3.2%)	1.00
Neurologic dysfunction	1 (2.3%)	0 (0%)	1 (3.3%)	1.00
Ischemic stroke	1 (2.3%)	0 (0%)	1 (3.2%)	1.00
Hemorrhage stroke	2 (4.5%)	0 (0%)	2 (6.5%)	1.00
Total thrombotic events	17 (38.6%)	4 (30.8%)	13 (41.9%)	0.74
DVT	16 (36.4%)	3 (23.1%)	13 (41.9%)	0.31
PE	2 (4.5%)	0 (0%)	2 (6.5%)	1.00
Ischemic digits	4 (9.1%)	1 (7.7%)	3 (9.7%)	1.00
Ischemic bowel	1 (2.3%)	0 (0%)	1 (3.2%)	1.00
AKI	24 (54.5%)	6 (46.2%)	18 (58.1%)	0.52
Dialysis	14 (31.8%)	4 (30.8%)	10 (32.3%)	1.00
Sepsis	24 (54.5%)	4 (30.8%)	20 (64.5%)	0.05

Note: Continuous data are shown as means ± standard deviation (SD).

Abbreviations: AKI, acute kidney injury; AMPAC, Activity Measure for Post-Acute Care; DVT, deep vein thrombosis; GI, gastrointestinal; PE, pulmonary embolism.