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Pediatric patients on veno-arterial extracorporeal membrane oxygenation undergoing cardiac rehabilitation have better outcomes

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BACKGROUND: The importance of physical rehabilitation in optimizing outcomes in critically ill patients is recognized. However, the frequency and benefit of mobilization in pediatric patients undergoing veno-arterial (VA) extracorporeal membrane oxygenation (ECMO) are unclear. This study evaluates a cohort of pediatric VA-ECMO patients to characterize the spectrum of mobility and evaluate associations of mobilization with clinical outcomes.
METHODS: We analyzed 688 patients (8-18 years) who underwent primary ECMO runs and had mobilization data collected in the Extracorporeal Life Support Organization Registry. Demographics, pre-ECMO support, location and duration of support, and outcomes, including survival to hospital discharge, heart transplant, and ECMO-related complications, were collected. Propensity score modeling was performed with entropy weighting to compare outcomes between mobile and nonmobile patients.
RESULTS: Of the 688 patients included, 10% achieved some degree of mobility (69/688); the majority of those exercised in bed. After propensity score matching, mobility was associated with an increased likelihood of being discharged alive (odds ratio (OR) 1.16, 95% cardiac index (CI) 1.04, 1.30) and receiving a heart transplant (OR 1.15, 95% CI 1.02, 1.29), and a lower likelihood of dying on ECMO

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(OR 0.90, 95% CI 0.81, 1.00). There was no association between mobility and ECMO being discontinued due to complication (OR 1.03, 95% CI 0.97, 1.10).
CONCLUSION: Mobilization in a pediatric VA-ECMO cohort was achieved by 1/10 patients, is associated with heart transplant and survival to hospital discharge, and is not associated with ECMO-related adverse events. Mobility in certain pediatric VA-ECMO patients is feasible and may represent an opportunity to improve outcomes.
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Background

The importance of physical rehabilitation in optimizing outcomes in critically ill patients is increasingly being recognized,[1-11] with the 2022 Society of Critical Care Clinical Practice recommending early mobility programming in all pediatric patients cared for in intensive care units (ICUs).[12] This recommendation is based on evidence that mobility may reduce ICU delirium,[13] shorten hospital length of stay,[14] and accelerate the ultimate development of functional mobility.[15] Historically, concerns about patient safety largely prohibited mobility in patients supported with extracorporeal membrane oxygenation (ECMO); however, recent work has demonstrated the feasibility of mobilizing patients on veno-venous (VV) ECMO, with the suggestion that mobility may be associated with improved outcomes.[16-26] While veno-arterial (VA) ECMO remains a critical therapy in the care of pediatric patients with refractory cardiorespiratory failure, there are limited data describing the frequency and distribution of mobility, or evaluating the association of mobilization with outcomes. Thus, the aims of this study are 3-fold: firstly, to characterize the spectrum of mobilization of pediatric patients supported on VA ECMO in a large heterogenous cohort; secondly, to evaluate the associations of mobility with survival to hospital discharge and heart transplant in pediatric patients supported on VA ECMO; and finally, to evaluate the association of mobility with ECMO-related complications in pediatric patients supported with VA ECMO.

Methods

Data source and study population

The Extracorporeal Life Support Organization (ELSO) Registry was queried for all patients aged 8-18 years undergoing a primary run of VA ECMO from January 1, 2018, through June 16, 2021. Patients who received extracorporeal cardiopulmonary resuscitation were not included in the study cohort, as this was thought to be a qualitatively different population. The start date coincided with the time at which ELSO began collecting mobility data on patients supported with ECMO, and the conclusion date was chosen to allow for a follow-up period of at least 1 year for all subjects included. Mobility data are not recorded by ELSO in patients younger than 8 years old. For patients older than 8, ELSO includes 2 data entry fields related to mobility: maximum mobility score and level of mobilization at 7 days of ECMO support. We chose maximum mobility score as our primary exposure of interest in order to include those patients on ECMO for < 7 days. There were several patients who had a value recorded for level of mobilization at day 7 but no maximum mobility score. Given the possibility of data entry error, an inability to verify if these scores were in fact the maximum level of mobility, and that this was not our primary exposure of interest, these patients were not included in the study population. Patients with values in both fields were included and assigned based on maximum mobility score (i.e., a patient with a maximum mobility score of 2 and day 7 score of 0 was included in the mobile cohort).

Main outcomes, measures, and statistical analyses

Demographic information, pre-ECMO support, cannulation strategy (central vs peripheral), location of support (cardiac intensive care unit (CICU) vs pediatric intensive care unit (PICU)), and duration of support data were collected. Primary diagnoses, a defined field in the ELSO database with a single possible value for each subject, were collected for all encounters and then categorized as cardiomyopathy/heart transplant complication, congenital heart disease, sepsis/infection, and other. For subjects with nonspecific primary diagnoses (i.e., cardiogenic shock), secondary diagnoses were used to sort them into the above categories. The frequency of mobilization was described by center to evaluate center associated practice differences. The primary study outcome was survival to hospital discharge, with secondary outcomes including transition to ventricular assist device, heart transplant or heart-lung transplant, and ECMO-related complications. Mobility was recorded by ELSO using a 10-point scoring system ranging from nothing (lying in bed) (0) to walking independently without a gait aid (10) (Table S1). Patients were then stratified into nonmobile (score of 0) and mobile groups (all other scores). All subjects had data on mobilization status and the 4 outcomes of interest. Missingness among covariates was rare (< 7% for all), except for cannulation strategy (12.4%). Only complete data were used to complete the adjusted analysis. Unweighted analysis was performed with Student's *t*-test and Wilcoxon signed-rank test as appropriate for the normality of the data. Propensity score modeling with entropy weighting was applied to the mobile and nonmobile groups to balance the distribution of confounders between them. The propensity score represents the probability of an individual being assigned to either the mobile or nonmobile group, based on observed baseline characteristics or confounders. This model allows us to design and analyze an observational (nonrandomized) study in a way that simulates a randomized controlled trial. The outcomes, weighted by the propensity score, were compared for each of the 4 outcomes of interest. Entropy weighting assigns weights to each individual based on the entropy balance principle. This principle aims to minimize the weighted difference in covariate distributions between groups, thus achieving balance. The weights are calculated in such a way that they maximize the

Table 1 Demographic and Clinical Characteristics of Study Population

Characteristic	Nonmobile (N = 619)	Mobile (N = 69)	Overall (N = 688)	*p*-value
Age (years)	13.6 [8.00, 17.9]	14.9 [8.00, 17.9]	13.8 [8.00, 17.9]	0.075
Weight (kg)	50.0 [3.29, 200]	52.0 [16.5, 133]	50.0 [3.29, 200]	0.808
Sex				0.376
Female	296 (47.8%)	29 (42.0%)	325 (47.2%)	
Male	323 (52.2%)	40 (58.0%)	363 (52.8%)	
Duration of support (days)	4.6 [0, 75.0]	6.5 [1.6, 61.7]	4.8 [0, 75.0]	0.016
Location				< 0.001
Cardiac ICU	598 (96.6%)	53 (76.8%)	651 (94.6%)	
Mixed ICU	16 (2.6%)	15 (21.7%)	31 (4.5%)	
Cardiac arrest prior to ECMO	224 (36.2%)	13 (18.8%)	237 (34.4%)	0.017
Primary diagnosis				< 0.001
Sepsis/infection	76 (12.3%)	6 (8.7%)	82 (11.9%)	
Cardiomyopathy/post-transplant complication	80 (12.9%)	12 (17.4%)	92 (13.4%)	
Congenital heart disease	94 (15.2%)	5 (7.2%)	99 (14.4%)	
Myocarditis	54 (8.7%)	19 (27.5%)	73 (10.6%)	
Other[a]	301 (48.6%)	27 (39.1%)	328 (47.7%)	
Cannulation strategy				0.017
Central	197 (31.8%)	14 (20.3%)	211 (30.7%)	
Peripheral	340 (54.9%)	43 (62.3%)	383 (55.7%)	
Unknown	6 (1.0%)	3 (4.3%)	9 (1.3%)	
Pre-ECMO support				
Pulmonary vasodilator	90 (14.5%)	10 (14.5%)	100 (14.5%)	1.000
Mechanical circulatory support	118 (19.1%)	11 (15.9%)	129 (18.8%)	0.520
Narcotics	361 (58.3%)	30 (43.5%)	391 (56.8%)	0.008
Neuromuscular blockade	296 (47.8%)	17 (24.6%)	313 (45.5%)	< 0.001
Pacemaker	36 (5.8%)	8 (11.6%)	44 (6.4%)	0.116
Renal replacement therapy	40 (6.5%)	6 (8.7%)	46 (6.7%)	0.457
Vasoactive medications	524 (84.7%)	61 (88.4%)	585 (85.0%)	0.822

Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.
Values are displayed as either median [Min, Max] or N (%).
[a]Other includes shock not otherwise specified (NOS), heart failure NOS, poisoning, arrhythmia, respiratory failure, hematologic, and pulmonary hypertension.

entropy (or randomness) subject to the constraint that the weighted distributions of covariates are similar across the groups. Variables included in building the propensity score model were determined a priori using a literature review and are included in Table 1. Statistics were performed using R version 4.1.3.

Results

There were 788 patients, ages 8-18 years, identified as being supported with a primary run of VA-ECMO from January 1, 2018, to June 16, 2021. There were 99 patients who did not have a maximum mobility score recorded and were therefore removed from the study population. A single patient was supported on VA ECMO for 258 days (6194 hours) and was treated as an outlier and removed from the study cohort, leaving 688 patients available for analysis. Key baseline clinical and demographic characteristics of the 688 subjects in both the nonmobile and mobile groups are included in Table 1. The median weight of patients in the cohort was 50.0 kg, 53% were male, and the median duration of ECMO support was 4.8 days. A history of congenital heart disease was found in 14.4% of patients, while 13.4% had cardiomyopathy and 10.6% had myocarditis. The vast majority of patients (94.6%) were cared for in a dedicated CICU as opposed to a combined CICU/PICU, and slightly more than half of the patients were cannulated peripherally. About 1/3 (34.4%) of patients had a history of a cardiac arrest prior to being placed on ECMO, more than half (57%) were on narcotics, 46% under neuromuscular blockade, and 85% on vasoactive medications prior to being placed on ECMO.

Ten percent (69/688) of patients achieved some mobility (Figure 1) with most of those mobile patients (81%, 56/69) reaching a maximum mobility score which corresponded to participating in exercises while seated in bed. When comparing mobile to nonmobile patients, there was no difference in median age or weight. Mobile patients had a longer duration of ECMO support (6.5 vs 4.6 days, $p = 0.016$) and a lower incidence of cardiac arrest prior to ECMO (18.6% vs 36.2%, $p = 0.014$). Mobile patients were more likely to have a diagnosis of cardiomyopathy or myocarditis (17.4% and 27.5% vs 13.4% and 10.6%) and less likely to have congenital heart disease (7.2% vs 14.4%, $p \leq 0.001$). They were more frequently cared for in mixed ICUs (21.7% vs 2.6% $p < 0.001$), more frequently cannulated peripherally (62.3% vs 54.9%, p = 0.0.17) and less likely to be on narcotics (43.5% vs 58.3% $p = 0.008$) or treated with

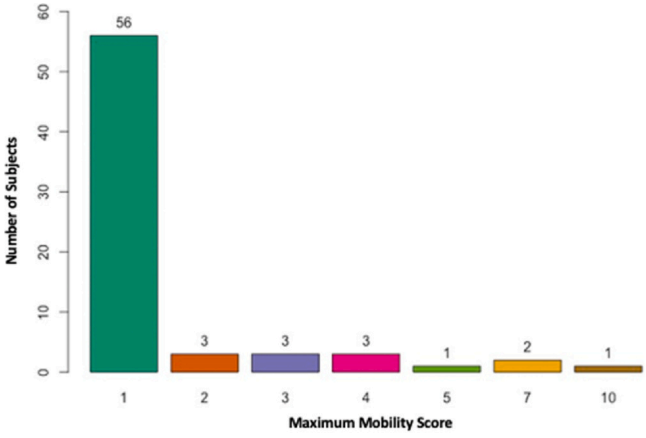

Figure 1 Distribution of maximum mobility score: 69 of the 688 patients in the study cohort achieved some measure of mobility with the majority of those performing exercises while seated in bed.

neuromuscular blockade (24.6% vs 47.8% $p < 0.001$). Additional modalities of pre-ECMO support were similar between both mobile and nonmobile patients.

Figure 2 shows the frequency of mobilization by center. Each of the 195 contributing centers is included on the x axis and the frequency of mobilization is shown on the y axis (i.e., a score of 1.0 = all subjects were mobile, 0.0 = no subjects were mobile, and 0.5 = half the subjects are mobilized). The number of included subjects each center contributes to the overall cohort is plotted. As an example, center 100 had 2 subjects, one of which was mobilized (frequency of.50), while center 184 had 4 subjects, one of which was mobilized (frequency of 0.25). There was statistically significant center-level variation in the frequency of mobilization as demonstrated in the corresponding figure. Unadjusted outcomes, shown in Table 2, varied significantly between groups with a greater proportion of mobile than nonmobile patients being discharged alive from their ECMO hospital admission (82.6% vs 65.1% $p = 0.003$) or receiving a heart or heart-lung transplant (21.7% vs 9.7% $p = 0.003$). There was no statistically significant difference between the presence or absence of mobility and the frequency of hemolysis, circuit thrombosis, circuit change, cannulation site bleeding, or ECMO support being discontinued to a complication. A greater proportion of patients who remained nonmobile during their period of ECMO support ultimately had withdrawal of life-sustaining therapy (22.5% vs 13.0%, $p = 0.049$). Differences between the 2 groups both before and after propensity score modeling are presented in Table 3, with a standardized mean difference ≥0.1 suggesting a substantial difference (highlighted in red). After using entropy weighting, there was excellent balance between the mobile and nonmobile groups with no significant differences remaining (all standardized mean differences now < 0.1).

In the matched cohorts, mobility was significantly associated with an increased likelihood of being discharged alive (OR 1.16, 95% cardiac index (CI) 1.04, 1.30), receiving a heart transplant (OR 1.15, 95% CI 1.02, 1.29), and a lower likelihood of dying on ECMO support (OR 0.90, 95% CI 0.81, 1.00). In the adjusted model, there remained no association between maximum mobility score and likelihood of ECMO being discontinued because of an ECMO-related complication (OR 1.03, 95% CI 0.97, 1.10) (Figure 3).

Discussion

This article demonstrates the feasibility and potential importance of cardiac rehabilitation in critically ill pediatric patients on VA ECMO. To the best of our knowledge, this is the largest epidemiologic analysis of mobility in a pediatric cohort of VA ECMO patients, and there are several significant findings. Firstly, 1 out of 10 children included in

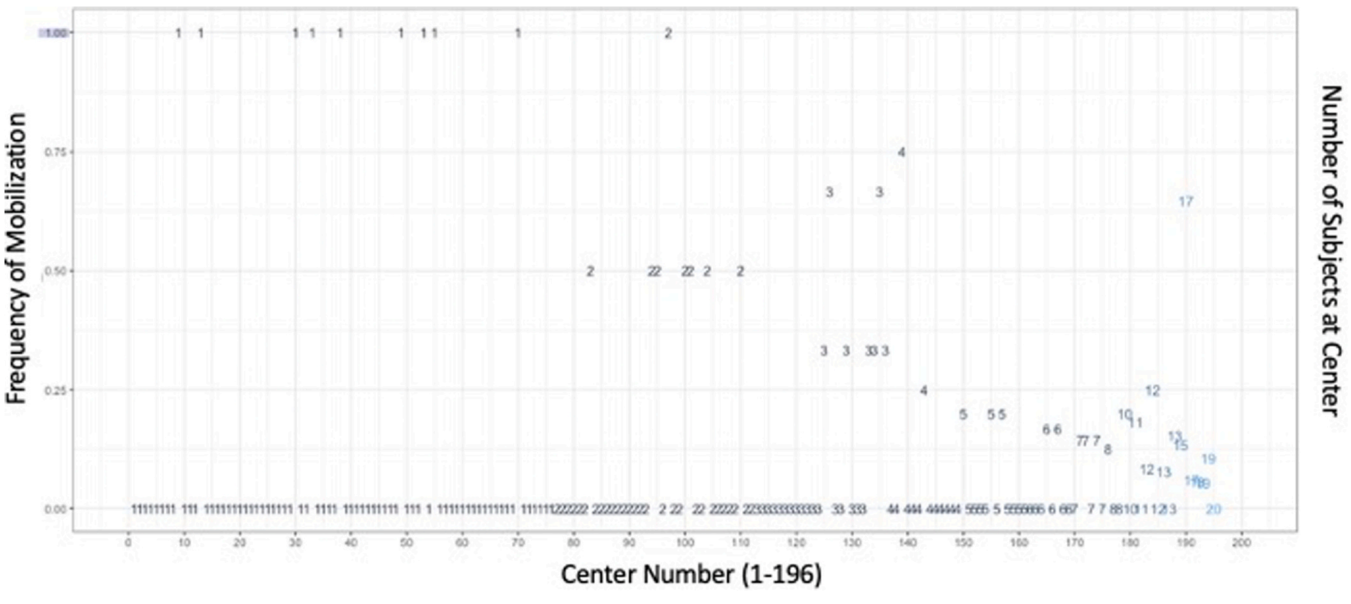

Figure 2 Frequency of mobilization by center. There was significant variation in institutional practices, with certain centers mobilizing the majority of their patients, and others avoiding mobilization entirely.

Table 2 Unadjusted Outcomes

Characteristic	Nonmobile (N = 619)	Mobile (N = 69)	Overall (N = 688)	*p*-value
Discharged alive	403 (65.1%)	57 (82.6%)	460 (66.9%)	0.003
Transplant	60 (9.7%)	15 (21.7%)	75 (10.9%)	0.003
Complications				
Moderate hemolysis	19 (3.1%)	2 (2.9%)	27 (3.9%)	1
Severe hemolysis	22 (3.6%)	1 (1.4%)	26 (3.8%)	0.569
Circuit thrombosis	53 (8.6%)	9 (13.0%)	69 (10.0%)	0.312
Circuit change	44 (7.1%)	7 (10.1%)	58 (8.4%)	0.502
Cannulation site bleeding	128 (20.7%)	10(14.5%)	153(22.2%)	0.290
ECMO discontinued				0.095
Withdrawal of life sustaining technology	146 (23.6%)	9 (13.0%)	155 (22.5%)	0.049
Complication	10 (1.6%)	2 (2.9%)	12 (1.7%)	0.343
Transplant	15 (2.4%)	5 (7.2%)	20 (2.9%)	0.041
VAD	45 (7.3%)	6 (8.7%)	51 (7.4%)	0.629

Abbreviations: ECMO, extracorporeal membrane oxygenation; VAD, ventricular assist device.

this large nationally representative cohort of pediatric VA ECMO patients achieved some level of mobilization while on ECMO. Secondly, those who achieved mobilization were more likely to survive to hospital discharge or receive a heart transplant, even after adjusting for illness severity. Thirdly, patients in the mobility cohort did not have an increased risk of ECMO-related complications. Finally, there was significant center level variation with mobility far more commonly achieved in a mixed ICU setting compared to a dedicated CICU.

Roughly 1 in 10 patients in this cohort achieved some measure of mobility while supported by VA ECMO. While this rate is substantially lower than that seen in other critically ill pediatric populations, including those requiring mechanical ventilation,[3] and also lower than the adult VA ECMO population,[23] our data demonstrate that performing physical rehabilitation in pediatric VA ECMO patients is feasible and is taking place. Interestingly, and perhaps surprisingly, nonmobile and mobile patients generally had similar markers of pre-ECMO illness severity with comparable rates of pulmonary vasodilator use, support with systemic vasopressors, and other mechanical circulatory support. However, patients achieving mobility were less frequently receiving sedation with narcotics and neuromuscular blockade prior to ECMO. While this study is not able to assess whether the decreased use of sedating medications or neuromuscular blockade allowed for participation in cardiac rehabilitation, other studies have demonstrated the caustic effect of sedation in critically ill children, including those on ECMO.[27-33] Our results may support limiting exposure to sedatives and neuromuscular blockade, when it is safe and appropriate to do so, it may help contribute to successful cardiac rehabilitation in children on VA ECMO. In other populations of critically ill children, sedation protocols have been found to limit sedative use without adverse outcomes. Whether similar protocols are safe and effective in pediatric ECMO patients, and ultimately facilitate mobilization, is an important area for future study.[1]

Importantly, for most in this cohort, mobility involved performance of exercises while still in bed. Few patients achieved out-of-bed mobility with 7 standing out of bed and only 3 ambulating. We hypothesize that current barriers to mobilizing pediatric VA ECMO arise from concerns regarding patient safety, as well as the resource-intensive nature involved in implementing such measures. The fact that even modest degrees of physical therapy was associated with clinical benefit has important implications, as this may be more easily achieved by intensive care teams than full ambulation. These results could suggest that even a subtle change in the current practice model, from keeping the majority of VA ECMO patients immobilized to including in-bed exercises as the new standard of care, may have positive clinical consequences.

The patients in the mobile cohort were more likely to survive to hospital discharge or receive a heart transplant than nonmobile patients. Mechanisms for such a relationship in other critically ill populations have been proposed and include reductions in muscle atrophy, ICU delirium, and cardiopulmonary deconditioning, and these results suggest that these benefits may extend to patients on VA ECMO. Given the unacceptably high rate of mortality in VA ECMO patients, the identification of potentially modifiable risk factors is especially important. In evaluating these results, it is important to acknowledge that patient-level factors can never be entirely accounted for in a nonrandomized study design, nor can the current study assess causality. However, the mobile and nonmobile groups were extremely well matched after propensity score matching, and these positive clinical associations persisted in the adjusted analysis. The findings of this study should motivate prospective investigation to definitively characterize whether achievement and degree of mobility while on VA ECMO modifies patients' clinical courses and confers a reduction in morbidity and mortality.

Perhaps the foremost barrier to mobilization in VA ECMO patients is the concern that doing so will lead to

Table 3 Differences Between Groups Before and After Propensity Matching

Characteristic	Before Propensity Score Weighting: SD Mean	After Propensity Score Weighting: SD Mean
Weight (Kg)	0.08	0.02
Duration of Support (Hours)	0.38	0.04
Location: Mixed ICU	0.63	0.01
Cardiac Arrest Prior to ECMO	0.42	0.01
Primary Diagnosis: Cardiomyopathy/ Post-Transplant Complication		
Congenital Heart Disease	0.27	0.01
Myocarditis	0.58	0.03
Sepsis/Infection	0.09	0.06
Other	0.34	0.00
Cannulation Strategy: Central		
Peripheral Cannulation	0.22	0.02
Unknown	0.18	0.01
Pre-ECMO Support		
Pulmonary Vasodilator	0.01	0.04
Mechanical Circulatory Support	0.09	0.05
Narcotics	0.38	0.01
Neuromuscular Blockade	0.58	0.02
Pacemaker	0.20	0.00
Renal Replacement Therapy	0.06	0.00
Vasoactive Medications	0.07	0.00

Standardized mean differences ≥0.1 suggest a substantial difference (highlighted in red).
Table 3 is matched based on the primary study outcome: discharged alive.

ECMO-related complications. However, in this cohort, participation in mobility programming was not associated with an increased rate of ECMO-related adverse events. Safety of mobility programming has been demonstrated in other pediatric ICU populations,[5] including patients with severe traumatic brain injury,[34] and patients being supported by paracorporeal ventricular assist devices.[35] Mobility with an ECMO circuit involves a unique set of risks for device-associated complications, such as line thrombosis, hemolysis, air introduction to the circuit, and cannulation site problems. Encouragingly, the findings of this study suggest that mobility programming can be performed safely with appropriate patient selection. This is consistent with observations of mobility programming in adults on VA ECMO; reported safety events related to mobilization have been rare even with high rates of out-of-bed activity.[36]

Lastly, mobilization was observed more frequently in patients admitted to a mixed PICU/CICU setting than in patients in a dedicated CICU. One potential explanation is that this observation represents broader institutional differences. In our center-level analysis, we found significant variation in the frequency of mobilization by center with some institutions mobilizing most of their patients and others electing to avoid mobilization of VA ECMO patients completely. It is also possible that this finding is due to the influence of the increasingly common practice of mobilizing VV ECMO patients, who are traditionally cared for in PICUs.[16-26] As mixed

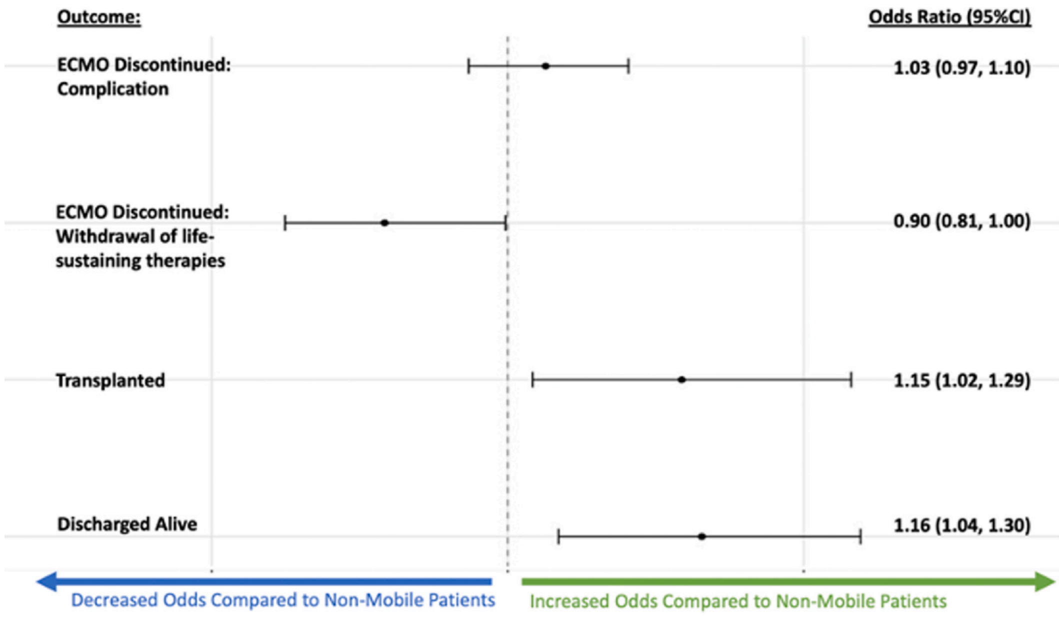

Figure 3 Association of mobility with clinical outcomes after propensity score weighting. Mobility was significantly associated with an increased likelihood of being discharged alive, receiving a heart transplant, and a lower likelihood of dying on ECMO support. There remained no association between mobility and likelihood of ECMO being discontinued due to complication.

units have developed an infrastructure which supports mobilizing VV ECMO patients and are able to appreciate those in whom it is both safe and beneficial, they may be extending this practice to those on VA ECMO support. Studies have shown the benefit of cross-disciplinary collaboration for the care of cardiac patients with severe acute kidney injury, and a similar approach could be effective in this care model as well, with "mobile ECMO support teams" including physicians, physical therapists, nurses, and perfusionists, spending time in both the PICU and CICU.[37-40] Ultimately, additional evaluation of this finding in an unblinded dataset that includes granular information about patient illness severity, the use of narcotics and neuromuscular blockade, and center size and staffing models could help to clarify the association of institutional management strategies on mobilization.

Limitations

This study has limitations inherent to the use of registry data for a retrospective study. While registry data offered us the opportunity to examine a large and heterogenous cohort of patients, it did not allow for granular analysis of patient-level characteristics or institutional practices that may determine the achievement or effect of mobility, nor does it capture the care teams' decision-making process as it pertains to mobilizing patients, or the frequency in which these patients were mobilized. Due to the retrospective nature of this study, we cannot comment on causality. While we attempted to control for patient-level factors using propensity scoring, it remains challenging to determine whether mobilization is a contributor to positive clinical outcomes or a result of clinical stability which independently associates with a positive outcome. As is the case in all retrospective studies, we can never completely account for confounding factors that may contribute to the outcomes of interest. Among the non-mobile cohort, 22.5% had withdrawal of life sustaining therapies, and therefore may not have had the opportunity to be mobilized. While our analysis included information regarding cannulation site, additional specifics of the cannulation strategies used, included direct cannulation vs graft, were not available in this data source and may influence whether patients can be mobilized. Thus, these results should inspire a future prospective analysis. Lastly, ELSO does not currently include mobility data on children younger than 8 years old, nor does it describe functional status prior to ECMO. Including these data elements in future iterations of the registry might increase the generalizability of the findings and better allow us to understand the trajectory of mobility in patients placed on ECMO.Those limitations noted, this study is novel in its scope and findings and offers significant contributions to the field.

Conclusion

This study contributes significantly to a growing body of evidence that cardiac rehabilitation and mobilization is an important component in the treatment of critically ill pediatric populations. In a sizeable pediatric cohort on VA ECMO, 1 in 10 patients successfully achieved mobilization. Furthermore, mobilization was linked to both heart transplantation and survival until hospital discharge, without any observed association with ECMO-related adverse events.

This may represent an important opportunity to improve function and survival in a population of critically ill pediatric patients, and these findings warrant further prospective inquiry to both establish whether a causal relationship exists between mobilization and clinical outcome and to identify which subgroups of VA ECMO patients would most benefit from mobilization.

Author contributions

All of the authors participated in the completion of this manuscript.

Disclosure statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jonathan Edelson reports a relationship with Abbott that includes consulting or advisory. Jonathan Edelson reports a relationship with AbioMed Inc. that includes consulting or advisory. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhlto.2024.100057.

References

1. Choong K, Canci F, Clark H, et al. Practice recommendations for early mobilization in critically ill children. J Pediatr Intensive Care 2018;7:14-26. https://doi.org/10.1055/s-0037-1601424.
2. Wieczorek B, Ascenzi J, Kim Y, et al. PICU Up!: impact of a quality improvement intervention to promote early mobilization in critically ill children. Pediatr Crit Care Med 2016;17:e559.
3. Betters KA, Hebbar KB, Farthing D, et al. Development and implementation of an early mobility program for mechanically ventilated pediatric patients. J Crit Care 2017;41:303-8.
4. Choong K, Awladthani S, Khawaji A, et al. Early exercise in critically ill youth and children, a preliminary evaluation: the wEECYCLE pilot trial. Pediatr Crit Care Med 2017;18:e546-54.
5. Abdulsatar F, Walker RG, Timmons BW, Choong K. "Wii-Hab" in critically ill children: a pilot trial. J Pediatr Rehabil Med 2013;6:193-204. https://doi.org/10.3233/PRM-130260.
6. LaRosa JM, Nelliot A, Zaidi M, Vaidya D, Awojoodu R, Kudchadkar SR. Mobilization safety of critically ill children. Pediatrics 2022;149:1-10.
7. Cuello-Garcia CA, Mai SHC, Simpson R, Al-Harbi S, Choong K. Early mobilization in critically ill children: a systematic review. J Pediatr 2018;203:25-33.e6. https://doi.org/10.1016/j.jpeds.2018.07.037.
8. Zhang L, Hu W, Cai Z, et al. Early mobilization of critically ill patients in the intensive care unit: a systematic review and meta-analysis. PloS One 2019;14:e0223185. https://doi.org/10.1371/journal.pone.0223185.
9. Tipping CJ, Harrold M, Holland A, Romero L, Nisbet T, Hodgson CL. The effects of active mobilisation and rehabilitation in ICU on mortality and function: a systematic review. Intensive Care Med 2017;43:171-83. https://doi.org/10.1007/s00134-016-4612-0.
10. Choong K, Canci F, Clark H, et al. Practice recommendations for early mobilization in critically ill children. J Pediatr Intensive Care 2018;7:14-26. https://doi.org/10.1055/s-0037-1601424.
11. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373:1874-82.
12. Smith HA, Besunder JB, Betters KA, et al. 2022 society of critical care medicine clinical practice guidelines on prevention and management of pain, agitation, neuromuscular blockade, and delirium in critically ill pediatric patients with consideration of the ICU environment and early mobility. Pediatr Crit Care Med 2022;23:e74-110.
13. Simone S, Edwards S, Lardieri A, et al. Implementation of an ICU bundle: an interprofessional quality improvement project to enhance delirium management and monitor delirium prevalence in a single PICU. Pediatr Crit Care Med 2017;18:531-40.
14. Tsuboi N, Hiratsuka M, Kaneko S, et al. Benefits of early mobilization after pediatric liver transplantation. Pediatr Crit Care Med 2019;20:e91-7.
15. Tsuboi N, Nozaki H, Ishida Y, et al. Early mobilization after pediatric liver transplantation. J Pediatr Intensive Care 2017;6:199-205.
16. Wells CL, Forrester J, Vogel J, Rector R, Tabatabai A, Herr D. Safety and feasibility of early physical therapy for patients on extracorporeal membrane oxygenator: University of Maryland Medical Center experience. Crit Care Med 2018;46:53-9.
17. Boling B, Dennis DR, Tribble TA, Rajagopalan N, Hoopes CW. Safety of nurse-led ambulation for patients on venovenous extracorporeal membrane oxygenation. Prog Transplant 2016;26:112-6.
18. Abrams D, Javidfar J, Farrand E, et al. Early mobilization of patients receiving extracorporeal membrane oxygenation: a retrospective cohort study. Crit Care 2014;18:1-9.
19. Abrams D, Javidfar J, Farrand E, et al. Early mobilization of patients receiving extracorporeal membrane oxygenation: a retrospective cohort study. Crit Care 2014;18:1-9.
20. Bonizzoli M, Lazzeri C, Drago A, et al. Effects of a physiotherapic program in patients on veno-venous extracorporeal membrane oxygenation: a 8 year single center experience. Minerva Anestesiol 2019:989-94.
21. Munshi L, Kobayashi T, DeBacker J, et al. Intensive care physiotherapy during extracorporeal membrane oxygenation for acute respiratory distress syndrome. Ann Am Thorac Soc 2017;14:246-53.
22. Zebuhr C, Sinha A, Skillman H, Buckvold S. Active rehabilitation in a pediatric extracorporeal membrane oxygenation patient. PM R 2014;6:456-60.
23. Abrams D, Madahar P, Eckhardt CM, et al. Early mobilization during extracorporeal membrane oxygenation for cardiopulmonary failure in adults: factors associated with intensity of treatment. Ann Am Thorac Soc 2022;19:90-8.
24. Hayes D, McConnell PI, Preston TJ, Yates AR, Kirkby S, Galantowicz M. Active rehabilitation with venovenous extracorporeal membrane oxygenation as a bridge to lung transplantation in a pediatric patient. World J Pediatr 2013;9:373-4.
25. Turner DA, Rehder KJ, Bonadonna D, et al. Ambulatory ECMO as a bridge to lung transplant in a previously well pediatric patient with ARDS. Pediatrics 2014;134:e583-5.
26. Lowman JD, Kirk TK, Clark DE. Physical therapy management of a patient on portable extracorporeal membrane oxygenation as a bridge to lung transplantation: a case report. Cardiopulm Phys Ther J 2012;23:30.
27. Harris J, Ramelet AS, van Dijk M, et al. Clinical recommendations for pain, sedation, withdrawal and delirium assessment in critically ill infants and children: an ESPNIC position statement for healthcare professionals. Intensive Care Med 2016;42:972-86.
28. Randolph AG, Wypij D, Venkataraman ST, et al. Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: a randomized controlled trial. JAMA 2002;288:2561-8.
29. Traube C, Silver G, Gerber LM, et al. Delirium and mortality in critically ill children: epidemiology and outcomes of pediatric delirium. Crit Care Med 2017;45:891.

30. Vet NJ, Ista E, de Wildt SN, van Dijk M, Tibboel D, de Hoog M. Optimal sedation in pediatric intensive care patients: a systematic review. Intensive Care Med 2013;39:1524-34.
31. Fonsmark L, Rasmussen YH, Carl P. Occurrence of withdrawal in critically ill sedated children. Crit Care Med 1999;27:196-9.
32. Ista E, van Dijk M, Gamel C, Tibboel D, de Hoog M. Withdrawal symptoms in children after long-term administration of sedatives and/or analgesics: a literature review. "Assessment remains troublesome". Intensive Care Med 2007;33:1396-406.
33. Burr JS, Jenkins TL, Harrison R, et al. The collaborative pediatric critical care research network critical pertussis study: collaborative research in pediatric critical care medicine. Pediatr Crit Care Med 2011;12:387-92.
34. Andelic N, Ye J, Tornas S, et al. Cost-effectiveness analysis of an early-initiated, continuous chain of rehabilitation after severe traumatic brain injury. J Neurotrauma 2014;31:1313-20.
35. Hollander SA, Hollander AJ, Rizzuto S, Reinhartz O, Maeda K, Rosenthal DN. An inpatient rehabilitation program utilizing standardized care pathways after paracorporeal ventricular assist device placement in children. J Heart Lung Transplant 2014;33:587-92.
36. Pasrija C, Mackowick KM, Raithel M, et al. Ambulation with femoral arterial cannulation can be safely performed on venoarterial extracorporeal membrane oxygenation. Ann Thorac Surg 2019;107:1389-94.
37. Askenazi DJ, Heung M, Connor Jr MJ, et al. Optimal role of the nephrologist in the intensive care unit. Blood Purif 2017;43:68-77.
38. Rewa OG, Villeneuve PM, Lachance P, et al. Quality indicators of continuous renal replacement therapy (CRRT) care in critically ill patients: a systematic review. Intensive Care Med 2017;43:750-63.
39. Rhee H, Jang GS, Han M, et al. The role of the specialized team in the operation of continuous renal replacement therapy: a single-center experience. BMC Nephrol 2017;18:1-9.
40. Oh HJ, Lee MJ, Kim CH, et al. The benefit of specialized team approaches in patients with acute kidney injury undergoing continuous renal replacement therapy: propensity score matched analysis. Crit Care 2014;18:1-9.