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Original Research

# Relationship of Age And Mobility Levels During Physical Rehabilitation With Clinical Outcomes in Critical Illness

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List of abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CCI, Charlson Comorbidity Index; FCI, Functional Comorbidity Index; ICU, intensive care unit; IMS, ICU Mobility Scale; LOS, length of stay; MICU, medical intensive care unit; MV, mechanical ventilation; OR, odds ratio; ROC-M, rate of change in mobility; SOFA, Sequential Organ Failure Assessment.

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*Measurements and Main Results:* Sample included 132 patients with 60 (45%) classified as younger (18-59 years) and 72 (55%) as older (60+ years). The most common diagnosis was sepsis/septicemia (32.6%). Older relative to younger patients had a significantly slower rate of improvement in ICU Mobility Scale (IMS) scores across rehabilitation sessions (mean slope coefficient 0.3 vs 0.6 points, P<.001), were less likely to be discharged to home (30.6% vs 55.0%, P=.005), and were more likely to die within 12 months (41.7% vs 25.0%, P=.046). Covariate-adjusted models indicated greater early improvement in IMS scores were associated with discharge home (P=.005). Longer time to first rehabilitation session, lower initial IMS scores, and slower improvement in IMS scores were associated with increased ICU days (all P<.03).

*Conclusion:* Older age and not achieving the mobility milestone of sitting at edge of bed or limited progression of mobility across sessions is associated with poor patient outcomes. Our findings suggest that age and mobility level contribute to outcome prognostication, and can aide in clinical phenotyping and rehabilitative service allocation.

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Adults admitted to the intensive care unit (ICU) for acute critical illness are at a high risk for physical complications, including muscle weakness,<sup>1</sup> functional decline,<sup>2</sup> prolonged need for mechanical ventilation (MV), and mortality.<sup>3</sup> Impairments acquired in the ICU can precipitate long-term physical, mental, and social debility and poor quality of life.<sup>4-8</sup> For example, nearly one-third of critical illness survivors who were employed prior to their illness will never return work,<sup>9</sup> and an estimated 50% will require daily care from a caregiver at some point during their recovery.<sup>10</sup> Survivorship is often accompanied by frequent hospital readmissions and higher secondary health care costs.<sup>11-13</sup> Older adult survivors are particularly at risk for longterm impairments and poor outcomes.<sup>14-20</sup> For instance, the use of life support with MV can lead to persistent cognitive impairment and dependence in activities of daily living.<sup>5,14</sup> Moreover, the presence of frailty prior to illness is associated with post-hospital institutionalization and mortality.<sup>21</sup> Taken together, age, comorbid status, and acute illness burden are important variables in the clinical spectrum of post-critical illness disability.<sup>22</sup> Therefore, critical care should emphasize development and/or optimization of therapeutic interventions that mitigate the negative sequelae of critical illness with goal-concordant care,<sup>23</sup> particularly for those individuals at highest risk of poor outcomes.

Physical rehabilitation in the ICU is safe and feasible across the adult age spectrum, and an emphasis on reducing the initial immobilization period has been purported to mitigate functional decline, reduce ventilation days and ICU and hospital lengths of stays, and potentially improve quality of life.<sup>24-37</sup> However, recent, larger randomized controlled trials comparing protocolized early mobilization and physical rehabilitation interventions with standard care have failed to show immediate or long-term benefits on primary endpoints.<sup>35,38-41</sup> Cautious interpretations of these findings are warranted because of the complexity of critical illness, the heterogeneity of enrolled patient populations and rehabilitation protocols delivered, and changes in standard care operating procedures. Further, standard care rehabilitation is frequently reported only as a dichotomous variable (yes or no), and patient functional status in and across rehabilitation sessions are rarely reported-neither of which allows quantification or assessment of therapeutic and physiological effect.

We hypothesize that age and patient-level physical function factors, including the highest level of mobility achieved in physical rehabilitation sessions and change in mobility level across the early sessions, are important variables influencing clinical outcomes. Risk stratification that includes mobility level may enhance outcome prognostication and goal-concordant care while improving the allocation of limited resources in the ICU, including rehabilitation services. Also, quantifying the initial mobility level and the early response to rehabilitation may further contribute to clinical phenotyping, better identify patients who can benefit from continued rehabilitative service, and lead to an individualized approach to rehabilitation.<sup>42,43</sup> Therefore, the primary purpose of this study is to determine whether age, mobility level, and rate of change in mobility level across early rehabilitation sessions delivered in a real-world clinical context have an effect on patient outcomes of length of stay, discharge disposition, and mortality.

## Methods

#### Design and patient population

The study is a retrospective cohort study of patients who were admitted to the Medical Intensive Care Unit (MICU) at an academic medical center over a 1 year duration. The center has 925 licensed beds with 24 MICU beds housed in a single ICU. Patients eligible for inclusion were (1) admitted to the MICU; and (2) participated in 3 or more consecutive physical rehabilitation sessions with a daily mobility assessment completed and documented in the electronic health record. Physical rehabilitation sessions included treatment provided by a physical therapist alone or accompanied with an occupational therapist. To mitigate the detrimental effects of immobility, treatment included passive range of motions exercises, active range of motion exercises, muscle resistance training, body positioning, functional mobility and transfers, cycle ergometry, or any combination of the aforementioned as functional and physiological status permited. If a patient was readmitted during the selected time frame, only data from the first admission was analyzed. A total of 132 patients were identified from the

electronic health records who met the eligibility criteria. The 132 patients were stratified into 2 groups based on age: (1) younger were 18-59 years of age; and (2) older were age 60 or greater. The study was approved by the Institutional Review Board of the health care system. Informed consent process was waived (exempt status) because of the retrospective study design.

#### Patient characteristics

Patient characteristics included demographics and clinical measures of critical illness severity and comorbid burden. Age, sex, race, body mass index (BMI), admitting diagnosis, rehabilitation session data, and preadmission health status using the Functional Comorbidity Index and the Charlson Comorbidity Index (CCI) were assessed. Higher scores on Functional Comorbidity Index and CCI indicate a worse preexisting comorbid burden. Severity of illness was assessed at admission using the Acute Physiology and Chronic Health Evaluation II<sup>44</sup> and Sequential Organ Failure Assessment (SOFA)<sup>45,46</sup> scores. Higher Acute Physiology and Chronic Health Evaluation II scores correspond to greater severity of disease or illness and a higher risk of mortality (score range: 0 to 71), while higher SOFA scores indicate higher risk for morbidity and mortality due to sepsis (score range: 0 to 24). Rehabilitation variables of interest included time from admission to first rehabilitation session and the highest level of mobility achieved. Mobility level was assessed during each rehabilitation session using the ICU Mobility Scale (IMS). The IMS was selected to track change in mobility status over the course of critical illness given its high interrater reliability (0.80),<sup>47</sup> validity, and responsiveness.<sup>48,49</sup> The IMS had a possible range of 0 to 10, with higher scores representing greater mobility.

## Patient outcomes

Clinical outcomes were MICU length of stay (LOS) in days, hospital LOS in days, discharge disposition, in-hospital mortality, 28-day mortality, and 12-month mortality. Discharge disposition included home/home service, skilled nursing facility, and long-term acute care, with each coded as 0=no or 1=yes.

#### Statistical analysis

Descriptive statistics were used to detail patient characteristics and key variables. Non-directional statistical tests were performed with significance set at 0.05. SAS version 9.4<sup>a</sup> software was used to conduct the analyses.

Independent *t* tests and Wilcoxon Two-sample tests for continuous measures as well as chi-square tests for categorical variables were used to test for age group (older vs younger) differences in patient characteristics and identify potential covariates for the outcome analyses.

Hierarchical random coefficients regression models for longitudinal data (a type of mixed-effects model for repeated measurements) were applied to assess the effect of age on the trajectories of change in IMS scores over the initial 3 rehabilitation sessions and estimate the rate of change over sessions within each age group. The initial 3 rehabilitation sessions were selected as the indicator of time so as to focus on the clinical effect of "early" rehabilitation interventions on patient outcomes. The trajectory model included the fixed effects of age group, time, and their interaction as well as the random effects of patient and patient-by-time. The missing at random assumption was met and a linear pattern of change was indicated. The model was also used to determine the average rate of change in mobility (ROC-M) per patient based on each patient's estimated trajectory of IMS scores (individual's slope coefficient) across the 3 sessions. Finally, *a priori* contrasts using independent *t* tests were performed to compare age group differences in adjusted means for IMS scores at each session and ROC-M.

Bivariate and multivariable (covariate-adjusted) regression models were used to explore the relationship between age group and patient outcomes. Initial covariates for the multivariable models were patient characteristics for which the age groups significantly differed as well as IMS scores at the first rehabilitation session and ROC-M due to their potential influence on outcomes. Each initial multivariable model was reduced to a final parsimonious model using a manual interactive backward elimination approach in which age group, regardless of statistical significance, and only covariates significant at the 0.05 level were retained in the final model. Logistic regression was applied for binary outcomes, while general linear regression was used for continuous outcomes. Effect sizes were estimated to explore the clinical significance, specifically odds ratios for binary outcomes and *r*-squared for continuous outcomes.

### Statistical power

The sample size of 132 patients that met eligibility (72 older, 60 younger) provided 80% statistical power for bivariate analyses to test for age group differences in patient characteristics and outcomes, assuming significance set at 0.05 for two-tailed test with medium effects (Cohen's d equivalent of 0.55). The sample size did not provide at least 80% statistical power for the initial covariate-adjusted regression models with 7 covariates for effect sizes in small to medium range. Thus, potentially clinically relevant covariates that were not statistically significant at the 0.05 due to low statistical power were removed from the final parsimonious model.

#### Results

#### Patient characteristics

Table 1 presents the demographic and clinical illness severity characteristics for the 132 patients in the total sample and by age group. Most patients identified as white (74.6%), and the most common admission diagnosis was sepsis/septicemia (32.6%) followed by respiratory disease or failure (24.2%). Patients were stratified into an older group (N=72) with a mean age of 69.6 years and younger age group (N=60) with a mean age of 45.0 years. The older group compared to the younger group had significantly fewer women (37.5% vs 60.0%, P=.010), lower BMI scores (median 26.4 vs 31.3 kg/

Table 1	Patient demographic and clinical characteristics	
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Characteristic	Total (N = 132)	Older (N = 72)	Younger (N = 60)	P value	
Age, in years	$\textbf{58.4} \pm \textbf{15.4}$	69.6 ± 7.0	45.0 ± 11.5	<0.001	
Female	63 (47.7%)	27 (37.5%)	36 (60.0%)	0.010	
White	97 (74.6%)	57 (80.3%)	40 (67.8%)	0.103	
Admission diagnosis					
Sepsis/septicemia	43 (32.6%)	25 (34.7%)	18 (30.0%)	0.564	
Pulmonary disease/failure	32 (24.2%)	14 (19.4%)	18 (30.0%)	0.159	
Transplant	13 (9.9%)	8 (11.1%)	5 (8.3%)	0.594	
Oncology/hematologic disease	13 (9.9%)	7 (9.7%)	6 (10.0%)	0.958	
Time to rehabilitation therapy, in hours	63.6 (20.5, 239.2)	47.8 (18.8, 120.2)	84.5 (37.2, 332.1)	0.029	
APACHE score at admission	18.3 ± 7.0	18.5 ± 6.1	18.1 ± 8.0	0.732	
SOFA score at admission	$\textbf{6.0} \pm \textbf{3.9}$	$5.3 \pm 3.3$	$\textbf{6.8} \pm \textbf{4.3}$	0.023	
BMI at admission, in kg/m <sup>2</sup>	27.6 (22.9, 33.9)	26.4 (22.5, 31.0)	31.3 (23.4, 38.5)	0.008	
BMI overweight/obese at admission	86 (65.2%)	43 (59.7%)	43 (71.7%)	0.152	
CCI score at admission	$5.2\pm2.9$	$\textbf{6.9} \pm \textbf{2.3}$	$3.3\pm2.3$	< 0.001	
CCI 10-year survival score at admission	21.4 (0.0, 77.5)	0.0 (0.0, 21.4)	77.5 (21.4, 95.9)	<0.001	
FCI score at admission	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	3.0 (2.0, 4.0)	0.139	
IMS score at first rehabilitation session	$\textbf{3.9} \pm \textbf{2.1}$	$\textbf{4.0} \pm \textbf{1.8}$	$\textbf{3.7} \pm \textbf{2.4}$	0.498	

NOTES: Mean  $\pm$  SD and independent *t* tests for age, APACHE, SOFA, CCI, and IMS scores; median (25th,75th percentile) and Wilcoxon Two-Sample Test for time to rehabilitation therapy, BMI, CCI 10-year survical, and FCI due to skewness of  $\pm$  1.0 or higher; n (%) and chi-square test for categorical measures. BMI overweight/obese class defined as a BMI of 25 kg/m<sup>2</sup> or greater. Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation II; FCI, Functional Comorbidity Index.

 $m^2$ , *P*=.008), lower SOFA scores (mean 5.3 vs 6.8, *P*=.023), and less time to rehabilitation therapy (median 47.8 vs 84.5 hours, *P*=.029), but higher CCI scores at admission (mean 6.9 vs 3.3, *P*<.001).

## Mobility trajectory analysis

Table 2 presents the adjusted mean IMS scores per session and average ROC-M across the 3 sessions that derived the trajectory model for the total sample and by age group. IMS scores significantly increased across the 3 rehabilitation sessions (time effect: P<.001) and the adjusted mean ROC-M was 0.4 points, indicating that on average the IMS scores improved by 0.4 points from session to session. However, age group (P=.209) and its interaction with time (P=.164) were not significantly associated with IMS scores. A priori contrasts indicated no age group differences in the mean adjusted IMS scores at each session, but the older group had a significantly different pattern and slower rate of improvement over time compared to the younger group (ROC-M adjusted mean 0.3 vs 0.6 points, P<.001). Although both groups had a similar rate of improvement from session 1 to 2, older patients did not continue to improve from session 2 to 3 relative to the younger patients who continued to improve by another 0.6 points on average.

#### Bivariate analyses: age group and patient outcomes

Bivariate regression models results (table 3) indicated older relative to younger patients were less likely to be discharged to home (30.6 % vs 55.0%, odds ratio [OR]=0.36, P=.005), but were more likely to die within 12 months (41.7% vs 25.0%, OR=2.14, P=.046). Age group was not significantly related to MICU or hospital LOS nor in-hospital or 28-day mortality.

## Multivariable analyses: age group and patient outcomes

The initial multivariable regression models with age group adjusted for 7 covariates: sex, time to rehabilitation therapy, and IMS scores at first rehabilitation session, along with

Table 2         Trajectory analysis: ICU mobility scale scores over rehabilitation sessions							
Assessment	Total (N=132) Adjusted Mean $\pm$ SD	Older (N=72) Adjusted Mean $\pm$ SD	Younger (N=60) Adjusted Mean $\pm$ SD	A priori contrast P value			
Time 1: Rehabilitation Session 1	$\textbf{3.9} \pm \textbf{1.5}$	$\textbf{4.0} \pm \textbf{1.3}$	$\textbf{3.7} \pm \textbf{1.7}$	0.366			
Time 2: Rehabilitation Session 2	$4.4\pm2.0$	$\textbf{4.6} \pm \textbf{1.8}$	$\textbf{4.3} \pm \textbf{2.2}$	0.824			
Time 3: Rehabilitation Session 3	$\textbf{4.8} \pm \textbf{1.8}$	$\textbf{4.6} \pm \textbf{1.6}$	$\textbf{4.9} \pm \textbf{1.9}$	0.663			
ROC-M: Rate of change in mobility	$\textbf{0.4}\pm\textbf{0.4}$	$0.3\pm0.3$	$\textbf{0.6} \pm \textbf{0.4}$	<0.001			

NOTES: Means of adjusted scores derived from the trajectory analysis; *P* value for *a priori* contrasts comparing older and younger patients using independent *t* tests.

Abbreviations: ROC-M, rate of change in mobility per patient indicated by the slope coefficient from the trajectory estimated for each patient.

Table 3 Descriptive statisti	cs and bivariate re	gression. age	group an	u patient c	Juccomes	S (N-132)			
Binary Outcome	Total n (%)	Older n (%)	Young	er n (%)	Wald ;	C <sup>2</sup> OR	OR 95%	CI	P value
Discharge Disposition									
Home/home service	55 (41.7%)	22 (30.6%)	33 (55	5.0%)	7.86	0.36	0.18, 0	.74	0.005
Skilled nursing facility	18 (13.6%)	13 (18.1%)	5 (8.	3%)	2.51	2.42	0.81,7	.24	0.113
Long-term acute care	17 (12.9%)	10 (13.9%)	7 (11	.7%)	0.14	1.22	0.44, 3	.43	0.705
Mortality									
In-hospital	27 (20.5%)	16 (22.2%)	11 (18	3.3%)	0.30	1.27	0.54, 3	.00	0.582
28-day	36 (27.3%)	24 (33.3%)	12 (20	).0%)	2.89	2.00	0.90, 4	.45	0.090
12-month	45 (34.1%)	30 (41.7%)	15 (25	5.0%)	3.98	2.14	1.01, 4	.53	0.046
Continuous Outcome	Total Median (25th, 75th)	Older Med (25th, 75t		Younger N (25th, 75t		b (SE)	b	R <sup>2</sup>	P value
MICU length of stay Hospital length of stay	9.9 (5.7, 16.1) 21.9 (13.5, 33.1	( )	,	12.8 (5.5, 24.4 (15.3	,	-0.15 (0.21) -0.01 (0.24)	-0.07 -0.00	0.07 0.00	0.382 0.988

 Table 3
 Descriptive statistics and bivariate regression: age group and patient outcomes (N=132)

NOTES: Logistic regression for binary outcomes; bivariate regression for continuous outcomes. Natural log of continuous outcomes used in regression models due to severe right skewness. Younger group = reference group for regression models.

Abbreviations: 95% CI, 95% confidence interval for odds ratio; b, unstandardized coefficient; b, standardized coefficient.

ROC-M, CCI, SOFA, and BMI at admission. We did not include CCI 10-year survival score at admission to avoid multicollinearity with CCI score at admission. The initial covariateadjusted model for each outcome was reduced to a final model that included age group and statistical significant covariates only (tables 4 and 5). The final models indicated that older patients compared to younger patients were less likely to discharge to home with or without home services (adjusted OR, [aOR]=0.47, P=.056) and were at higher risk for mortality in 12 months (aOR=2.14, P=.046). Age group was not significantly associated with any other outcomes (all P>.05). Higher IMS scores (better mobility) at the first rehabilitation session were associated with discharge to home with or without home services, and were related to a lower risk for discharge to long-term acute care (aOR=0.63, P=.010) and shorter MICU LOS (b=-0.23, P=.006). Greater rates of early improvement in mobility were associated with discharge to home with or without home services (aOR=4.91, P=.005) and decrease in MICU length of stay (b= -0.17, P=.030). Longer time to first rehabilitation session was associated with longer ICU LOS (b=0.04 P<.001), and hospital LOS (b=0.39, P<.001). A brief summary of regression results are provided in Supplemental Table 1 (available online only at http://www.archives-pmr.org/).

## Discussion

This study is a practice analysis demonstrating that age and mobility level achieved in physical rehabilitation sessions delivered in the ICU are associated with clinical outcomes. Our findings suggest that older age, higher comorbid burden, delayed time to initial rehabilitation session, lower mobility level at the initial rehabilitation session, and a slower rate of change in mobility level across the first 3 rehabilitation sessions are associated with poorer outcomes. Mobility level as a predictor of outcomes contributes to the mounting body of literature supporting classification of the heterogenous pool of patients with critical illness into clinical phenotypes based on patient demographics, clinical variables, and recovery markers<sup>50-52</sup> to aide in outcome prognostication, goal-concordant care discussions, and allocation of often

Table 4         Binary outcomes: final logistic regression model results							
Outcome	Explanatory Variable	Wald $\chi^2$	aOR	aOR 95% CI	P value		
Home/home service	Age group	3.60	0.47	0.22, 1.03	0.056		
	IMS score at first rehabilitation	3.82	1.20	1.0, 1.44	0.051		
	ROC-M	7.98	4.91	1.63, 14.80	0.005		
Skilled nursing facility	Age group	0.018	1.09	0.30, 4.0	0.894		
	CCI	4.74	1.26	1.02, 1.56	0.029		
Long-term acute care	Age group	3.00	3.20	0.86, 11.95	0.083		
	BMI at admission	9.03	1.07	1.03, 1.12	0.003		
	IMS score at first rehabilitation	6.72	0.63	0.44, 1.89	0.010		
In-hospital mortality	Age group	0.30	1.27	0.54, 3.00	0.582		
28-day mortality	Age group	2.88	2.00	0.90, 4.45	0.090		
12-month mortality	Age group	3.98	2.13	1.01, 4.53	0.046		

NOTES: Explanatory variables entered into model in descending order (highest to lowest); age group=older group (1) relative to younger group (0).

Abbreviations: aOR, adjusted OR; 95% CI, 95% confidence interval.

Outcome	Explanatory Variable	b	SE	t-value	P value	Adjusted R <sup>2</sup>
MICU length of stay						0.38
	Age group	-0.04	0.13	-0.56	0.571	
	Time to rehabilitation therapy, in hours	0.04	0.00	5.10	<0.001	
	IMS score at session 1	-0.23	0.03	-2.75	0.006	
	ROC-M	-0.17	0.18	-2.11	0.030	
Hospital length of stay						0.16
	Age group	0.75	0.13	0.92	0.369	
	Time to rehabilitation therapy, in hours	0.39	0.00	4.69	<0.001	

NOTE: Natural log of continuous outcomes evaluated in regression models due to severe right skewness. R2 adjusted for the overall model.

Abbreviation: b, standardized beta coefficient.

limited resources in the ICU including rehabilitation services. Together, these findings provide valuable insights into the patient experience of serious illness and may help explain the variances that exist in patient outcomes.

Table 5 Continuous outcomes: final multiple regression model results

Physical rehabilitation in the ICU is a recommended standard component of patient care.<sup>53</sup> Several studies demonstrate that either earlier initiation or increased frequency of physical rehabilitation sessions are associated with reduced ICU and hospital LOS,<sup>28,54-56</sup> greater likelihood of discharge to home,<sup>57,58</sup> and maybe improved long-term quality of life.<sup>31,35</sup> In our cohort, time to rehabilitation initiation was significantly associated with MICU and hospital LOS. Less attention in the field, however, has been given to mobility levels achieved during rehabilitation as an indicator of dose, and perhaprs a crude marker of intesnity. Recently, members of our team demonstrated that a steeper, positive change in mobility over the first 4 rehabilitation sessions in patients requiring extracorporeal membrane oxygenation was associated with survival and discharge to home.<sup>52</sup> Similarly, this current analysis indicates that a positive mobility trajectory over the first 3 sessions is associated with shorter ICU LOS and discharge to home. Notably, the change in mobility had a large effect on discharge to home. Also, a longer time to rehabilitation initiation and an inability to sit edge of bed (<3 IMS) at the initial rehabilitation session were associated with longer ICU and hospital LOS. The data may suggest that sitting upright at edge of bed is an important recovery milestone. Our data must be interpreted cautiously as we cannot draw causal inference from the study design. Also, the severity of illness leading to ICU admission as well as the underlying comorbid burden could influence the delay to rehabilitation and progress in each individual session. Simply, patients with higher severity of illness and worse preexisting health may not have positive outcomes regardless of rehabilitation delivery.

However, taken together, our studies provide seminal evidence that mobility level and mobility trajectory in the context of real-world ICU rehabilitation are at least associated and may be strong predictors of patient outcomes. This information may be useful in goal-concordant care discussions where clinicians provide prognostic information to the patient or their surrogate(s) for understanding the expected effect of critical illness and treatments on patient survival and functional outcomes.<sup>23</sup> In parallel, mobility trajectory across early rehabilitation sessions provides clinicians with objective data that can assist with tailoring service allocation. For example, a patient with a small, but positive ROC-M during the first 3 sessions may benefit from shorter, more frequent rehabilitation sessions to optimize mobility and outcomes. Mobility trajectory may be a useful additional component in clinical phenotyping to promote individualized medicine and rehabilitation care delivery.

Despite differences in illness severity and comorbid burden, mobility level gradually improved from the first to third rehabilitation session in both groups. However, the older group had a slower rate of change from the second to third rehabilitation session compared to the younger group. These data suggest that a different trajectory of illness and recovery may exist by age. To that end, the dosing of rehabilitation (mode, frequency, duration, intensity) may need to be tailored to age given that older adults have a higher risk of mortality, even with controlling for severity of illness and prexisting morbidity, 16,59-61 and likely respond differently to rehabilitation compared to younger adults. Despite the near decade-long explosion of studies in ICU rehabilitation, data on rehabilitation dosing parameters beyond timing and frequency are limited.<sup>62-64</sup> In fact, recent clinical practice guidelines recommend physical rehabilitation in ICU<sup>65</sup> but are devoid of recommendations on dosing parameters. A difference in trajectory of illness and recovery may also be related to ICU exposures. For instance, older patients tend to receive less intensive treatment in the ICU, including less use of MV, circulatory support, and renal support, even after adjustments for severity of illness and do not resuscitate status,<sup>66</sup> confounding the prediction of mortality solely due to age.<sup>60</sup> Whether less intensive intervention for patients with older age extends to physical rehabilitation dosing is not known. Future research should examine if rehabilitation service allocation and dosing in the ICU is influenced by demographics such as age as well as social determinants of health. A recent study suggests that referral to and receipt of rehabilitation is significantly reduced for patients of Hispanic identity.<sup>67</sup> Elucidating whether disparities exist in ICU rehabilitative care and developing mitigation strategies to address those should be given high priority by clinicians and scientists alike.

#### Study limitations

This study has several key strengths including evaluation of an age-diverse population of patients hospitalized in a large academic MICU with documented clinical and mobilityspecific variables. Further, using the novel approach of assessing rate of mobility change, we established the importance of mobility as a patient outcome. In addition, we used the IMS score, which has a high clinical utility and is a timeefficient approach to assess changes in mobility levels.47 The IMS has high inter-rater reliability,<sup>47</sup> excellent responsiveness with low floor and ceiling effects,<sup>68</sup> and high validity.<sup>48,69</sup> This study is limited by its retrospective design, which precludes establishing a causal association between exposures and outcomes. Also, the small sample size prevents the ability to perform complex regression modeling while controlling for known confounders. Thus, we emphasized the regression analyses as exploratory to guide future hypotheses and we also included adjusted and r-squared values to represent clinical significance. Our a priori approach to the statistical modeling was selected to optimize statistical power while recognizing our variable selection methods may inadequately control for confounders.<sup>70</sup> Secondarily, sparse documentation in the electronic health record precluded examination of frailty or nutritional status, which have been purported to affect clinical and functional outcomes.<sup>21,71</sup> Details regarding post-hospital care and rehabilitation, which could also confound long-term mortality, were not available. We decided a priori against stratifying mobility levels in an ordinal fasion, but classification by pattern of trajectory (positive, no-response, negative) may have allowed us to better examine change in mobility on mortality outcomes.

## Conclusions

Age, time to first rehabilitation session, initial mobility staus, and the change in mobility across early rehabilitation sessions are related to clinical outcomes of patients experiencing critical illness in the MICU. Knowledge of mobility levels and change therein may contribute to outcome prognostication, and thus aide in clinical phenotyping and rehabilitative service allocation.

## Supplier

a. SAS version 9.4 software; SAS Institute Inc

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