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Factors Associated with Timing of Initiation of Physical Therapy In Acute Lung Injury Patients

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Abstract

Objectives—Early initiation of physical therapy (PT) in mechanically ventilated patients is associated with improved outcomes. However, PT is frequently delayed until after extubation or discharge from the intensive care unit (ICU). We evaluated factors associated with the timing of initiation of PT in acute lung injury (ALI) patients admitted to ICUs without an emphasis on early rehabilitation.

Design—Secondary analysis of a prospective cohort study.

Settings—11 ICUs in 3 teaching hospitals.

Patients—503 ALI patients.

Interventions—None

Measurements and main Results—Thirty-four percent of patients ever received PT. In multivariable analysis, factors associated with later PT were a higher SOFA score (hazards ratio (HR) 0.89, 95% CI 0.85–0.93), higher FiO₂ (0.97, 0.96–0.98), mechanical ventilation (0.31, 0.16–0.59), coma (0.32, 0.20–0.51), delirium (0.72, 0.50–1.03) and continuous sedation (with daily sedation interruption (DSI): 0.49, 0.30–0.81; without DSI: 0.59, 0.39–0.89). Factors associated

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with earlier PT were an admitting diagnosis of trauma (3.31, 1.74–6.31) and hospital study site (2.84, 1.89–4.26).

Conclusions—In 11 ICUs without emphasis on early rehabilitation, ALI patients frequently received no PT. Severity of illness, mental status, sedation practices, and hospital site were significant barriers to initiating PT. Understanding these barriers may be important when introducing early ICU physical rehabilitation.

Keywords

Acute lung injury; critical illness; intensive care unit; mechanical ventilation; physical therapy; rehabilitation

Introduction

Mechanically ventilated patients are at risk for ICU-acquired weakness (ICUAW) from prolonged bed rest and inactivity, pharmacologic agents, and other critical illness neuromuscular abnormalities¹²³⁴. In 25% to 65% of ICU patients who are mechanically ventilated for at least 5 days, clinically significant neuromuscular weakness is present, which prolongs mechanical ventilation duration, and ICU and hospital stay¹⁵⁶⁷⁸⁹. In particular, acute lung injury (ALI) survivors commonly have muscle wasting and weakness, with long-lasting impairments in exercise capacity and physical function¹⁰¹¹.

When started early after initiation of mechanical ventilation, rehabilitation therapy has been associated with several benefits, including improved exercise capacity and functional status at hospital discharge, decreased duration of mechanical ventilation and ICU and hospital stay, and decreased hospital readmission and death in the first year after respiratory failure¹²¹³¹⁴¹⁵¹⁶¹⁷. However, despite evidence demonstrating its feasibility and safety in mechanically ventilated patients¹⁴¹⁵¹⁸¹²¹⁹, patient-, ICU-, and hospital-level factors may affect the timing of rehabilitation therapy, with many patients having therapy delayed until around the time of extubation and ICU discharge¹³¹⁷²⁰²¹²².

Perceived barriers to physical rehabilitation of mechanically ventilated patients include inadequate staffing, over-sedation and patient discomfort, and concerns with dislodgement of devices or worsening physiologic parameters²²²³. However, empirical evaluation of these barriers has not been fully explored. Understanding barriers to rehabilitation and associated practice patterns in hospitals without emphasis on early ICU rehabilitation is important when introducing this evidence-based practice²⁴. The objective of this study was to evaluate the association of patient, ICU and hospital factors with the time to starting PT in a prospective cohort of mechanically ventilated ALI patients.

Materials and Methods

Study Population

We conducted a secondary data analysis of a prospective cohort study evaluating outcomes of ALI patients²⁵. A total of 514 consecutive study subjects enrolled between October 2004 and October 2007 from 11 ICUs at 3 teaching hospitals in Baltimore, Maryland were considered for this analysis. This study was approved by The Johns Hopkins Medicine Institutional Review Board X (NA_00041630) and the Institutional Review Boards at each participating site.

Patients were eligible for the study if they were mechanically ventilated adults (>18 years) with ALI as defined by the American-European Consensus Conference²⁶. Relevant

exclusion criteria included: 1) substantial exposure to ICU care before eligibility and study enrollment (i.e., > 5 days of mechanical ventilation before ALI); 2) high mortality risk unrelated to ALI (i.e., pre-existing illness with life expectancy <6 months), or a preexisting limitation in use of life support therapy other than an order for no resuscitation in the event of cardiac arrest (e.g., a “no vasopressors” order); or 3) significant barriers to outpatient follow-up (i.e., communication or language barrier, no fixed address).

Exposure Variables

The exposure variables were patient, ICU and hospital factors potentially influencing the timing of initiation of physical therapy in the ICU. Patient data was prospectively abstracted from participants’ medical records, including: demographics (age, gender, and race), body mass index (BMI), source of ICU admission, ICU admission diagnosis, and severity of illness at ICU admission (Acute Physiology and Chronic Health Evaluation (APACHE) II²⁷ score). On a daily basis, the following additional patient factors were evaluated: organ dysfunction (Sequential Organ Failure Assessment (SOFA)²⁸ score), mechanical ventilation status, FiO₂, positive end-expiratory pressure (PEEP), and coma and delirium status (assessed using the Richmond Agitation Sedation Score (RASS)²⁹ with coma defined as a RASS of -4 or -5, and the Confusion Assessment Methods for the ICU (CAM-ICU)³⁰, respectively).

ICU factors evaluated included daily sedation-related status (no sedation infusion, continuous infusion with interruption, and continuous infusion with no interruption). Hospital study site was also evaluated (site 1, 2, or 3).

Outcome Variable

The primary outcome variable was time to first PT session during patients’ index ICU admission for ALI. Data on physical therapy interventions were abstracted from standardized PT notes in the medical records. Physician referral was required for physical therapy interventions to be initiated.

Statistical Analysis

Descriptive statistics were calculated, and Wilcoxon rank-sum, Chi-square and Fisher’s exact tests were used, as appropriate, to compare the exposure variables across patients who received PT in the ICU. Evaluation of patient exposures continued until the earliest of the following end points: first day of PT, ICU discharge, or death. Patients were censored if PT was not received by ICU discharge.

In this analysis, death was explicitly recognized as a competing risk to receiving PT in the ICU (i.e., patients with greater severity of illness were more likely to die and less likely to receive PT)³¹. Hence, the association between the time to first PT (outcome variable) and the exposure variables was assessed using bivariable and multivariable Fine and Gray proportional sub-distribution hazards regression models³² with time-varying covariates. This modeling approach was used since it specifically can address the competing risk of death. The more commonly used Cox proportional hazards method for time-to-event analyses could not be used because patient mortality was not independent of receiving PT.

Exposure variables were included in the multivariable Fine and Gray model if they demonstrated a bivariable association with the outcome measure of $p \leq 0.10$. Variance inflation factors were used to confirm the absence of multi-collinearity in the final multivariable regression model. Residual plots were used to visually inspect the proportional hazards assumptions. Data analyses were performed with STATA 11.0 software (Stata Corporation, College Station, TX). Statistical significance was defined as 2-sided $p < 0.05$.

Results

Of 514 eligible patients, 11 (2%) were excluded because of incomplete data for at least one exposure variable on one ICU day. Patient characteristics for the 503 subjects analyzed are summarized in Table 1. Of these 503 subjects, 170 (34%) ever received PT in the ICU. A total of 496 PT sessions were provided in the ICU to all 170 subjects. The most common PT interventions (patients could have more than 1 intervention during a single PT session) were mobility activities (52%) followed by passive range of motion (PROM) (40%), and breathing exercises (10%). Among those who ever received PT, the median (IQR) number of PT sessions in the ICU and duration of each session was 2 (1, 4) and 35 (25, 45) minutes, respectively.

Significant findings of bivariable analysis of patients ever (vs. never) receiving PT in the ICU included: younger age, admission due to trauma, lower severity of illness, lower FiO₂ while mechanically ventilated, lower proportion of ICU days in coma and admission to hospital site 3 (Table 1).

In the multivariable analysis (Table 2), daily patient factors independently associated with later initiation of PT in the ICU were: higher SOFA score (hazard ratio [HR] 0.89, 95% CI 0.85–0.93) and FiO₂ (0.97, 0.96–0.98); and mechanical ventilation (0.31, 0.16–0.59). Later initiation of PT was also strongly associated with coma (0.32, 0.20–0.51) and was marginally associated with delirium (0.72, 0.50–1.03). An admission diagnosis of trauma (vs. respiratory) was associated with earlier PT (HR 3.31, 1.74–6.31). Moreover, among ICU and hospital factors, a continuous infusion of sedatives, irrespective of daily interruption, was associated with later PT (with daily interruption: 0.49, 0.30–0.81; without daily interruption: 0.59, 0.39–0.89). Among the 3 participating hospitals, study site was independently associated with earlier PT (site 3 vs. site 1, 2.84, 1.89–4.26). Figure 1 depicts this hospital-specific finding through comparison, by study site, of the estimated adjusted cumulative proportion of patients starting PT in the ICU.

Discussion

This prospective, observational study of physical rehabilitation in the ICU included 503 ALI patients from 11 ICUs at 3 hospitals without an emphasis on early ICU rehabilitation. The study demonstrated that exposure to physical rehabilitation was low, with only 34% of patients ever receiving PT in the ICU. Patient, ICU and hospital factors independently associated with later initiation of PT included non-trauma ICU admission diagnoses, severity of illness, infusions of sedatives, coma and delirium status, and hospital site.

In our study, patient-related factors associated with later initiation of PT were: daily markers for severity of illness (SOFA score, FiO₂ and mechanical ventilation status) and delirium/coma status. The severity of illness findings are consistent with a prior observational study, but we could not replicate the previous finding of gender differences in ICU rehabilitation²⁰. Although in the setting of research studies¹²¹³¹⁵¹⁹ or in ICUs with emphasis on early rehabilitation¹⁴¹⁸²⁰, physical rehabilitation in mechanically ventilated patients is safe and feasible, this multisite study indicates that in hospitals without an emphasis on early ICU rehabilitation, severity of illness is an important barrier to starting PT. Greater education, training and multidisciplinary collaboration between critical care and rehabilitation clinicians may be important to overcome this barrier³³ as subsequently has occurred in one of the study site hospitals which created a critical care physical medicine and rehabilitation program¹⁴²²³³³⁴³⁵³⁶.

The administration of continuous infusion of sedatives, irrespective of daily sedation interruption, was independently associated with a later start of PT. This finding expands

upon an earlier report that the use of sedatives, even intermittent administration, significantly decreased ICU ambulation by two-fold²⁰. Our findings also demonstrate that independent of sedation infusions, changes in mental status (i.e., coma and delirium) are important barriers. Strategies for overcoming such barriers include: (1) pairing rehabilitation with sedation interruptions¹³ (which did not specifically occur in these study sites) and (2) changing approaches to lighten sedation in mechanically ventilated patients¹⁴¹³³³³⁷.

Among study site ICUs, none had predefined criteria for initiation of PT and a physician referral was required before starting PT activities. This is a common practice in US hospitals. In fact, a national survey of PT utilization in ICUs across the US reported that the vast majority of hospitals (89%) required physician consultation to initiate PT for their ICU patients³⁸.

Moreover, even after adjusting for patient and ICU factors, a trauma ICU admission diagnosis and admission to hospital site 3 were significantly associated with earlier time to first PT. Both of these findings may reflect that differences in clinician attitudes and organizational culture are important mediators of delivering early rehabilitation in the ICU¹⁷¹⁸²⁰²¹. However, we also acknowledge that incomplete adjustment for confounding factors may have also contributed to these findings.

Our study has potential limitations. First, as an observational study, we cannot draw cause-effect conclusions from these associations. However, consistency with prior studies adds to the confidence in these results. Second, we report on activities performed by physical therapists only. It is possible that patients may have received additional mobilization from bedside nurses, respiratory therapists or family members; however, based on our anecdotal experience in the study site ICUs, such mobilization was very rare among this cohort of ALI patients. Third, we did not evaluate measures of ICU culture or organizational factors specifically relevant to PT activities (i.e., team work, PT staffing, rehabilitation equipment). Future qualitative and quantitative investigation into the role of ICU culture is important to further build on our results. Fourth, we did not collect safety and training data related to PT activities which may have played an important role in this population of critically ill ALI patients. Lastly, our findings may not be generalizable to other ICU populations and/or non-academic centers since our study enrolled exclusively patients with ALI with high severity of illness at 3 teaching hospitals during the 2004 – 2007 time period. With new research evidence and quality improvement efforts, our findings regarding the incidence of PT in the ICU and associated barriers may be changing; however, such change in practice can often be slow³⁹. Despite these limitations, our study is important as it prospectively evaluated patient, ICU, and hospital factors empirically associated with starting PT in the ICU, within hospitals without specialized ICU physical rehabilitation programs.

Conclusions

Our study demonstrates that mechanically ventilated ALI patients admitted to ICUs without emphasis on early rehabilitation do not receive timely PT. Patient severity of illness and coma/delirium status, ICU sedation practices, and hospital factors are significant barriers to initiating PT. Understanding these barriers may be important to successfully introducing evidence-based rehabilitation therapy into routine clinical practice in the ICU.

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Figure 1. Estimated adjusted cumulative incidence of initiating physical therapy in the intensive care unit, by study site^a

^a Estimates are adjusted for all variables included in the multivariable regression model presented in Table 2.

Table 1

Baseline characteristics, by ICU physical therapy status

	ALL n= 503	Ever PT n= 170 (34%)	Never PT n= 333 (66%)	p-value ^a
PATIENT FACTORS				
Age, median (IQR), y	52 (42, 63)	51 (40, 60)	53 (42, 64)	0.030
Male, n (%)	279 (55)	94 (55)	185 (56)	>0.99
White race, n (%)	301 (60)	105 (62)	196 (59)	0.565
BMI, median (IQR)	27 (23, 32)	28 (23, 33)	27 (23, 32)	0.176
ICU admission diagnosis, n (%)				<0.001
Respiratory, including pneumonia	277 (55)	88 (52)	189 (57)	
Gastrointestinal	71 (14)	27 (16)	44 (13)	
Sepsis, non-pulmonary	84 (17)	21 (12)	63 (19)	
Trauma	13 (2)	12 (7)	1 (0)	
Other	58 (12)	22 (13)	36 (11)	
APACHE II at ICU admission, median (IQR)	21 (16, 28)	19 (15, 26)	22 (17, 29)	0.003
Mean daily SOFA score, median (IQR)	5.0 (2.5, 9.0)	3.8 (2.0, 6.7)	5.9 (3.0, 10.0)	<0.001
Proportion of days on mechanical ventilation, median (IQR)	78 (60, 91)	78 (53, 91)	78 (60, 90)	0.420
Mean daily FiO ₂ , median (IQR)	50 (43, 62)	47 (42, 56)	52 (44, 67)	<0.001
Mean daily PEEP, median (IQR)	5.1 (3.8, 6.8)	5.0 (3.4, 6.6)	5.1 (3.8, 7.1)	0.112
Proportion of days with delirium/coma per patient, median (IQR)				
No delirium	0 (0, 23)	1 (0, 29)	0 (0, 20)	0.009
Delirium	29 (0, 55)	38 (16, 60)	22 (0, 50)	0.001
Coma	53 (22, 88)	44 (13, 67)	62 (33, 93)	<0.001
ICU FACTORS				
Median (IQR) proportion of days per patient, with:				
No sedation infusion	27 (0, 56)	23 (0, 56)	27 (4, 55)	0.246
Infusion with interruption	14 (0, 27)	17 (3, 30)	13 (0, 25)	0.004
Infusion without interruption	50 (27, 75)	49 (29, 71)	50 (27, 75)	0.563
HOSPITAL FACTOR				
Hospital, n (%)				<0.001
site 1	188 (38)	40 (24)	149 (45)	
site 2	162 (32)	38 (22)	124 (37)	
site 3	153 (30)	92 (54)	61 (18)	
DISCHARGE LOCATION ^b				<0.001
Death	227 (45)	32 (19)	195 (59)	
Home	108 (21)	40 (24)	68 (20)	
Facility	159 (32)	92 (54)	67 (20)	
Other	8 (2)	5 (3)	3 (1)	
STUDY YEAR				0.033
2005	155 (31)	41 (24)	114 (34)	
2006	200 (40)	69 (41)	131 (39)	
2007	148 (29)	60 (35)	88 (27)	

Abbreviations: APACHE, acute physiology and chronic health evaluation; BMI, body mass index; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; IQR, interquartile range; PEEP, positive end-expiratory pressure; PT, physical therapy; SOFA, sequential organ failure assessment

^acalculated using Pearson Chi-Squared, Fisher's exact, and Wilcoxon rank-sum tests, as appropriate

^bDischarge location was missing in 1 subject

Table 2Factors associated with time to initiating physical therapy in the ICU^a

	Bivariable			Multivariable		
	HR	CI	p	HR	CI	p
PATIENT FACTORS						
Age, y	0.98	(0.98, 0.99)	0.003	0.99	(0.98, 1.00)	0.134
Male	1.00	(0.74, 1.34)	0.989	0.93	(0.69, 1.25)	0.628
White race	1.09	(0.81, 1.47)	0.578	1.32	(0.95, 1.83)	0.093
BMI	1.00	(0.99, 1.02)	0.844	1.02	(1.00, 1.04)	0.080
ICU admission diagnosis						
Respiratory, including pneumonia	1.00			1.00		
Gastrointestinal	1.19	(0.79, 1.79)	0.415	0.86	(0.53, 1.49)	0.542
Sepsis, non-pulmonary	0.79	(0.49, 1.25)	0.313	0.89	(0.58, 1.37)	0.585
Trauma	7.35	(3.27, 16.51)	<0.001	3.31	(1.74, 6.31)	<0.001
Other	1.65	(1.02, 2.65)	0.040	1.54	(0.97, 2.44)	0.066
APACHE II score at ICU admission	0.96	(0.94, 0.97)	<0.001	1.02	(1.00, 1.04)	0.097
SOFA score	0.83	(0.80, 0.87)	<0.001	0.89	(0.85, 0.93)	<0.001
Mechanical ventilation	0.20	(0.14, 0.28)	<0.001	0.31	(0.16, 0.59)	<0.001
FIO₂	0.95	(0.94, 0.96)	<0.001	0.97	(0.96, 0.98)	<0.001
PEEP	0.95	(0.88, 1.02)	0.156	1.07	(0.99, 1.15)	0.094
Delirium/coma			<0.001			<0.001
No delirium	1.00			1.00		
Delirium	0.38	(0.26, 0.55)	<0.001	0.72	(0.50, 1.03)	0.069
Coma	0.09	(0.06, 0.13)	<0.001	0.32	(0.20, 0.51)	<0.001
ICU FACTORS						
Sedation infusion						
No sedation infusion	1.00			1.00		
Infusion with interruption	0.42	(0.26, 0.67)	0.001	0.49	(0.30, 0.81)	0.005
Infusion without interruption	0.33	(0.23, 0.46)	<0.001	0.59	(0.39, 0.89)	0.011
HOSPITAL FACTOR						
Hospital						

	Bivariable			Multivariable		
	HR	CI	p	HR	CI	p
Site 1	1.00			1.00		
Site 2	1.10	(0.72, 1.68)	0.654	0.86	(0.55, 1.32)	0.481
Site 3	4.20	(2.92, 6.03)	<0.001	2.84	(1.89, 4.26)	<0.001

Abbreviations: APACHE, acute physiology and chronic health evaluation; BMI, body mass index; CI, confidence interval; FiO2, fraction of inspired oxygen; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; PEEP, positive end-expiratory pressure; SOFA, sequential organ failure assessment

^a assessed using Fine and Gray proportional subdistribution hazards regression models,³⁴ with time-varying exposures for daily SOFA score, mechanical ventilation status, FiO2, PEEP, sedation interruption and delirium. Hazard ratios greater than 1 indicate an association with receiving PT earlier in the ICU.