ORIGINAL ARTICLE

A Randomized Trial of an Intensive Physical Therapy Program for Patients with Acute Respiratory Failure

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Abstract

Rationale: Early physical therapy (PT) interventions may benefit patients with acute respiratory failure by preventing or attenuating neuromuscular weakness. However, the optimal dosage of these interventions is currently unknown.

Objectives: To determine whether an intensive PT program significantly improves long-term physical functional performance compared with a standard-of-care PT program.

Methods: Patients who required mechanical ventilation for at least 4 days were eligible. Enrolled patients were randomized to receive PT for up to 4 weeks delivered in an intensive or standard-of-care manner. Physical functional performance was assessed at 1, 3, and 6 months in survivors who were not currently in an acute or long-term care facility. The primary outcome was the Continuous Scale Physical Functional Performance Test short form (CS-PFP-10) score at 1 month.

Measurements and Main Results: A total of 120 patients were enrolled from five hospitals. Patients in the intensive PT group received 12.4 $\pm$ 6.5 sessions for a total of 408 $\pm$ 261 minutes compared with only 6.1 $\pm$ 3.8 sessions for 86 $\pm$ 63 minutes in the standard-of-care group ($P < 0.001$ for both analyses). Physical function assessments were available for 86% of patients at 1 month, for 76% at 3 months, and for 60% at 6 months. In both groups, physical function was reduced yet significantly improved over time between 1, 3, and 6 months. When we compared the two interventions, we found no differences in the total CS-PFP-10 scores at all three time points ($P = 0.73$, 0.29, and 0.43, respectively) or in the total CS-PFP-10 score trajectory ($P = 0.71$).

Conclusions: An intensive PT program did not improve long-term physical functional performance compared with a standard-of-care program.

Clinical trial registered with www.clinicaltrials.gov (NCT01058421).

Keywords: acute respiratory failure; critical care; mechanical ventilation; physical therapy

Each year in the United States, more than 300,000 patients develop acute respiratory failure that requires mechanical ventilation and admission to an intensive care unit (ICU) (1). As a result of recent advances in critical care, mortality rates associated with acute respiratory failure continue to decline, and now over 80% of these patients survive their hospitalization (2). Therefore, improving long-term outcomes for these patients has become more clinically relevant. One of the most common and debilitating limitations for survivors of acute respiratory failure is exercise limitation and decreased physical quality of life that can persist up to 5 years after hospital discharge (3–8). These patients have difficulty lifting and carrying groceries, climbing stairs, bending, kneeling, walking moderate

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At a Glance Commentary

Scientific Knowledge on the Subject: Early physical therapy programs may benefit patients with acute respiratory failure; however, their proper duration and intensity is currently unknown.

What This Study Adds to the Field: We conducted a randomized controlled trial of 120 patients with acute respiratory failure and determined that an intensive physical therapy program did not improve long-term physical functioning compared with a standard-of-care physical therapy program.

distances, and performing other routine activities of daily living (3, 4).

Until recently, the management of critically ill patients, including those with acute respiratory failure, consisted of inactivity and bed rest for extended periods of time (5). Such prolonged immobility can result in significant muscle wasting (5). For patients with a variety of neuromuscular disorders, physical therapy (PT) programs can be effective in reducing neuromuscular dysfunction and weakness (9–13). PT programs may improve multiple aspects of physical function, including muscle strength, endurance, and the performance of functional activities (9). Depending upon their frequency, intensity, and duration, specific PT interventions may build muscle strength but do not always improve physical functional performance. Excessive exercise can also damage muscles and result in the loss of strength or "overwork weakness" (12). Therefore, the proper balance between insufficient and excessive PT can be difficult to determine.

Early PT programs may benefit patients with acute respiratory failure by preventing or attenuating ICU-acquired neuromuscular weakness (5, 14–20). Several observational studies involving patients with acute respiratory failure have demonstrated that early PT programs are both safe and feasible (21–23). However, only a few randomized clinical trials of early PT for these patients have been done, and they do not consistently support the efficacy of these interventions (24–26). In addition, in only one previous trial did researchers follow patients after hospital discharge and assess long-term functional outcomes (25). Furthermore, the authors of multiple systematic reviews have concluded that additional trials are needed to provide more robust evidence to support the efficacy of early PT interventions for patients with acute respiratory failure (14, 16, 17, 27, 28).

Because the proper duration and intensity of PT interventions for patients with acute respiratory failure are unknown, we conducted a randomized controlled trial to determine the efficacy of an intensive PT program in comparison with a standard-of-care PT program. We hypothesized that the intensive PT program would be associated with significant improvements in long-term measures of physical functional performance.

Methods

We recruited study participants from five medical centers in the Denver metropolitan area. All of these hospitals have access to long-term acute care hospitals. The institutional review boards for all the medical centers approved the study, and written informed consent was obtained from participants or their authorized representatives. The first subject was enrolled on August 7, 2009, and the last 6-month follow-up was conducted on October 17, 2,014.

The initial inclusion criteria were patients at least 18 years of age who required mechanical ventilation for at least 5 days. Because neuromuscular weakness is common after 4 days of mechanical ventilation, we expanded our inclusion criteria to include patients who required mechanical ventilation for 4 or more days (8). This protocol change was initiated on May 4, 2012, after 78 patients had been enrolled in the study. Exclusion criteria are included in the online supplement. The medical care for all enrolled patients was delivered by dedicated intensivists. The treating physicians managed all patients with evidence-based protocols, including sedation, ventilator management and weaning, insulin therapy, and electrolyte replacement (29–34).

Patients were randomized in a 1:1 ratio to an intensive PT program or to a standard-of-care PT program. Randomization occurred at the time of awakening defined by standard criteria (35). Initial neuromuscular function was determined using Medical Research Council Scale dyspnea scale scores, hand-grip strength by dynamometry, and Functional Independence Measure bed mobility scores (35–38). At each hospital, there were two distinct study teams: (*1*) intensive PT program therapists and (*2*) standard-of-care PT program therapists. The therapists chose their team assignment, and there was no overlap between these two groups. Patients received intensive or standard-of-care PT for up to 28 days. Patients who were hospitalized for more than 28 days received study-related treatment for only 28 days. After that time, the PT treatment was left to the discretion of the treating team. For patients transferred before Day 28 to a long-term acute care facility, a rehabilitation hospital, or a skilled nursing facility, the administration of PT and other forms of therapy was left to the discretion of the health-care professionals at that facility. All patients were tracked and followed for up to 6 months after study entry.

In the intensive PT program, therapy was conducted for up to 28 days after randomization or until the patient successfully completed all stages of the program. While a patient was an inpatient, PT was delivered 7 days per week by a licensed physical therapist. After hospital discharge to a home environment, the protocol was continued in the home or on an outpatient basis 3 days per week until the subject completed 28 days of therapy or was able to successfully complete all stages of the program. PT sessions were planned for 30 minutes while the patient was in the ICU and for up to 60 minutes while the patient was on a regular hospital floor, in an outpatient setting, or at home. The components of the PT program consisted of five elements delivered in a graduated manner: (*1*) techniques for proper breathing during exercise, (*2*) progressive range of motion, (*3*) therapeutic exercises emphasizing muscle strengthening, (*4*) exercises designed to improve core mobility and strength, and (*5*) functional mobility retraining, including bed mobility, transfers, gait, and balance. *See* the online supplement for more information on the intensive PT intervention.

The components of the standard-of-care PT program were based upon our

national survey that identified PT intervention practices for patients with acute respiratory failure (39). As inpatients, patients assigned to the standard-of-care PT program received range-of-motion exercises, positioning, and functional mobility retraining 3 days per week by a licensed physical therapist. Once participants were able, they were assisted in daily activities such as transfers to bedside or chair and ambulation in their room. Similarly to the patients in the intensive PT arm, standard-of-care patients received their intervention for up to a total of 28 days. However, at hospital discharge to home, these patients received only information on the importance of daily exercise and were encouraged to initiate their own exercise program. No formal outpatient therapy program was delivered to the patients receiving standard care. To avoid the occurrence of attention bias, patients in the standard-of-care arm received telephone calls 3 days per week to be given answers to any of their questions and to ensure that they were functioning well at home. *See* the online supplement for more information on the standard-of-care PT intervention. For patients receiving either intervention, we used established criteria for not initiating a session and safety criteria for the early termination of a PT session (*see* online supplement).

Our primary outcome variable was the short form of the Continuous Scale Physical Functional Performance Test (CS-PFP-10), used 1 month after study enrollment (40, 41). The CS-PFP-10 is used to assess an individual's overall capacity to carry out

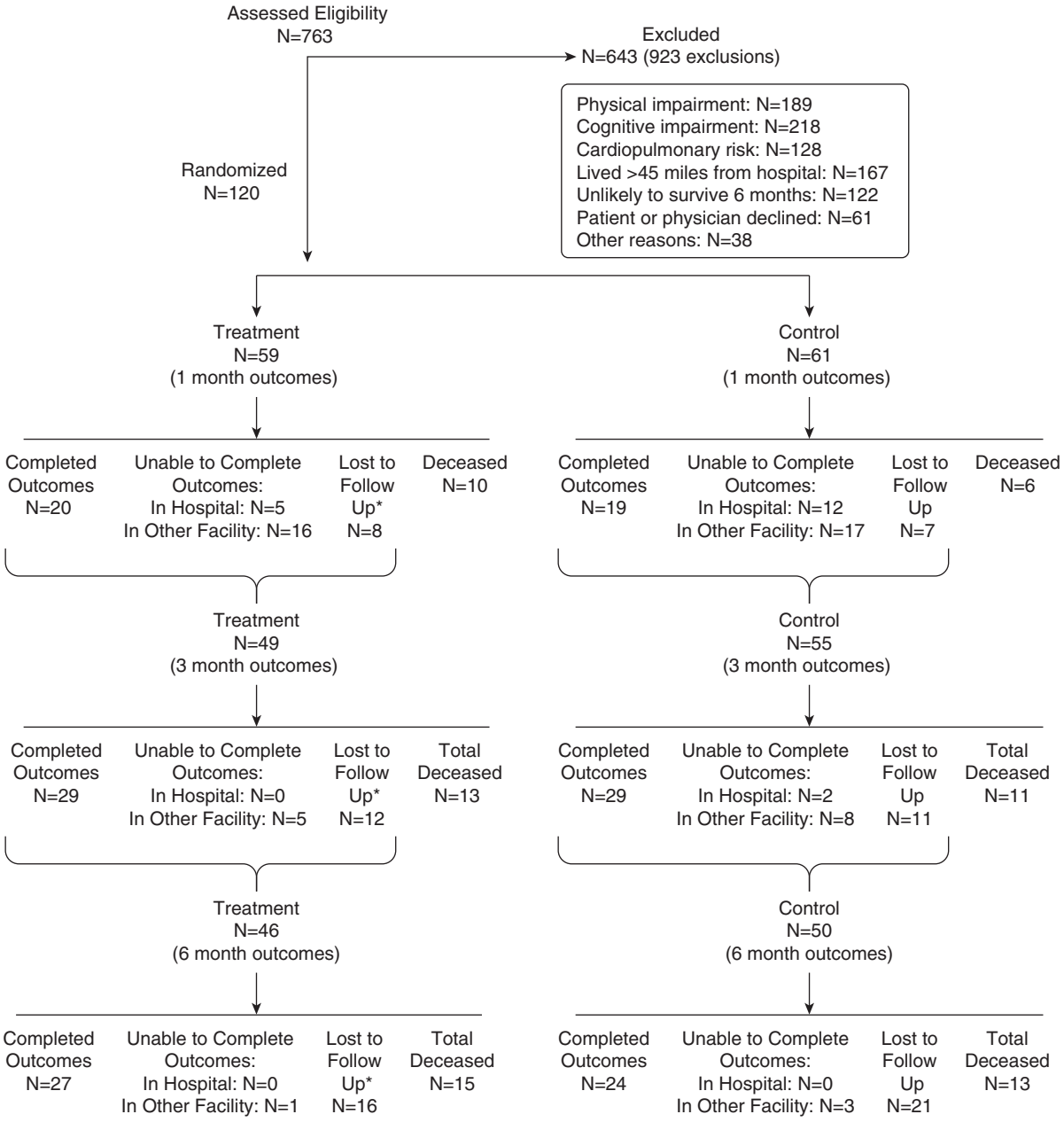

Figure 1. Consolidated Standards of Reporting Trials diagram. *Patients who elected not to participate in the follow-up studies are included here (n=3).

instrumental activities of daily living by measuring and quantifying 10 activities accomplished in a typical day, such as sweeping a floor, transferring clothes from a washer to a dryer, and carrying groceries. Tasks are quantified using time alone, time and weight, and distance. Because the tasks are performed sequentially, this test provides a realistic and practical measure of movement capacity and ability to accomplish sustained activity. The CS-PFP-10 provides an overall score and scores for upper body strength, upper body flexibility, lower body strength, balance and coordination, and endurance. The CS-PFP-10 was administered at 1, 3, and 6 months after study enrollment. If patients were in the hospital or in a long-term care facility at the time of their outcome assessment, they received a CS-PFP-10 score of 0. All outcome measures were performed in a standardized PT laboratory by a physical therapist formally trained in conducting the CS-PFP-10 and blinded to group assignment. In two *post hoc* subgroup analyses, CS-PFP-10 scores were stratified according to the presence or absence of preexisting comorbidities and by patient age tertiles (42).

Secondary outcome measures included ICU- and hospital-free days at Day 28, discharge to home, all-cause mortality at Day 28, and institution-free days at Day 90 and Day 180. Institution-free days were defined as alive and free of hospitalization or living in a long-term care, rehabilitation, or skilled nursing facility. For patients who were able to return for their follow-up outcome assessments, other measures of physical functional performance were also performed, including the Five Times Sit to Stand Test, the Timed Up and Go Test, the Berg Balance Test, and the 36-item Short Form Health Survey. These tests were similarly performed at 1, 3, and 6 months after study enrollment (*see* online supplement).

Previous studies indicated that clinically significant changes in the CS-PFP-10 are between 8–15 points with an estimated SD of 17.5 (41, 43, 44). Assuming mortality of 34% and a loss to follow-up rate of 11%, enrollment of 120 patients could detect a difference of 12.3 points between the group mean CS-PFP-10 score at 1 month with a significance level (α) of 0.05 and a power of 80% using a two-sided test (1–3, 45, 46). Longitudinally measured outcomes (e.g., CS-PFP-10) were analyzed using all available data in a repeated-measures mixed model (SAS PROC MIXED; SAS Institute, Cary, NC) with an unstructured covariance for the correlated repeated measures. We used *t* tests associated with linear contrast to assess differences at specific time points ($\alpha = 0.05$). This trial is registered with www.clinicaltrials.gov (NCT01058421).

Results

A total of 763 patients were assessed for eligibility, of whom 120 (15.7%) were enrolled and randomized into the study (Figure 1). The most common reasons for exclusion were baseline cognitive impairment (n = 218), cardiopulmonary risk factors (n = 128), and preexisting physical impairment (n = 189). Table 1 demonstrates the baseline characteristics of the enrolled subjects. All 120 study patients enrolled were living independently at home before hospital admission. Patients randomized to the standard-of-care group were younger (49 ± 15 yr vs. 56 ± 14 yr; $P = 0.01$) than the intensive intervention patients.

Awakening and randomization occurred at a median of 7 days after the initiation of mechanical ventilation (25–75% quartiles, 6–9 d). The median number of days from initiation of mechanical ventilation until the first PT session was 8 days (25–75% quartiles, 6–11 d). The median number of days from randomization until first PT session was 1 day (25–75% quartiles, 0–1 d). At the time of randomization, Medical Research Council Scale dyspnea scale scores, hand-grip strength, and Functional Independence Measure bed mobility scores could be determined for 86, 57, and 88 subjects, respectively. There were no differences between the two study groups for any initial

Table 1. Patient Demographics

	Intensive PT Patients (*n* = 59)	Standard-of-Care PT Patients (*n* = 61)	*P* Value
Sex, % male	61	57	0.69
Age, yr	56 ± 14	49 ± 15	0.01
APACHE II score	17.9 ± 6.2	17.4 ± 5.6	0.64
Service unit, % MICU	88	90	0.47
Pre-ICU location, %			
Emergency department	63	57	0.54
Standard hospital floor service	24	31	
Other	13	12	
Primary diagnosis, %			0.21
ARDS	32	26	
Pneumonia	17	31	
Nonpulmonary sepsis	22	18	
Aspiration	10	7	
Postoperative	2	7	
COPD exacerbation	0	5	
Other	17	6	
Prior residence, %			
Home	100	100	1.0
Assessment after randomization			
Medical Research Council dyspnea scale scores*	33.8 ± 13.4 (n = 43)	38.0 ± 15.6 (n = 43)	0.19
Hand grip strength, kg-force*	10.0 ± 9.2 (n = 30)	13.3 ± 10.6 (n = 27)	0.22
Functional Independence Measure bed mobility*	2.0 ± 1.2 (n = 45)	2.3 ± 1.6 (n = 43)	0.35

Definition of abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation II; ARDS = acute respiratory distress syndrome; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; MICU = medical intensive care unit; PT = physical therapy.
Age, APACHE II scores, and assessments after randomization are presented as mean ± SD.
*A normal Medical Research Council dyspnea scale score is 60. ICU-acquired weakness is defined as a Medical Research Council dyspnea scale score less than 48. Depending on an individual's age and sex, normal values for hand-grip strength range between 20 and 40 kg-force. The Functional Independence Measure bed mobility survey is scored on a 1–7 scale on which 1 means the patient needs total assistance to perform the bed mobility tasks and 7 means complete independence with no need for physical assistance or devices such as bed rails.

neuromuscular assessment measures (Table 1).

As part of the study protocol, patients received 1,233 PT sessions (Table 2). A total of 1,188 (97.3%) sessions were delivered in the acute care hospital, and a total of 45 (3.7%) sessions were delivered on an outpatient basis, including home visits. Patients in the intensive PT group received 12.4 ± 6.5 sessions compared with only 6.1 ± 3.8 sessions for patients in the standard-of-care group ($P < 0.001$). In the intensive PT and standard-of-care groups, patients received therapy on 78% and 88% of eligible study days, respectively ($P = 0.046$). Overall, 170 PT sessions were not delivered during the study period (average of 1.4 missed sessions per enrolled patient). The most common reasons for inability to perform a PT session were hemodynamic or respiratory instability (35%), altered mental status (32%), patient refusal (13%), current use of a paralytic agent (8%), and other reasons (12%).

The overall average duration for each PT session was 39.4 ± 11.0 minutes in the intensive PT group compared with 21.8 ± 3.5 minutes for patients in the standard-of-care group ($P < 0.001$). The intensity of PT activity was also significantly greater in the intensive PT group. For example, 73% (43 of 59) of intensive PT patients performed some form of standing exercises during their treatment period compared with only 15% (9 of 61) of patients in the control arm ($P < 0.001$) (Table 2). Overall, the total amount of time that patients in the intensive PT group received treatment was 408 ± 261 minutes compared with only 86 ± 63 minutes for patients in the control group ($P < 0.001$). During the hospital length of stay, only two patients receiving standard of care (2 of 61 [3%]) and no patients receiving intensive PT (0 of 59 [0%]) achieved functional independence before the end of their treatment period. For the intensive PT patients who were discharged to home, only 27% (3 of 11) achieved functional independence before the end of their 28-day treatment period.

Sedation and analgesia did not differ between the two groups, including the number of days receiving benzodiazepines, propofol, dexmedetomidine, or narcotics (Table 3). The average daily doses were also not different between the two groups of patients. In addition, the number of days that patients received neuromuscular blocking agents was not different between the two groups.

Overall, 13% (16 of 120) of patients died during their hospitalization. There was no difference between the groups regarding hospital mortality: 17% (10 of 59) in the intensive PT group compared with 10% (6 of 61) in the standard-of-care group ($P = 0.25$). All of the in-hospital deaths occurred in the ICU. There was also no difference between the two groups in 28-day ICU-free days or 28-day hospital-free days (Table 4). In regard to discharge status, there was no difference in the percentage of patients discharged to home between the intensive PT group 51% (25 of 49) compared with 49% (27 of 55) in the standard-of-care group ($P = 0.84$).

Assessments of physical functioning were available for 86% (89 of 104) of patients at 1 month, 76% (73 of 96) at 3 months, and 60% (55 of 92) at 6 months. In both groups, the total CS-PFP-10 scores increased significantly over time from 1 to 3 months and from 3 to 6 months ($P < 0.01$ for all analyses). However, there were no differences in the overall trajectory of the total CS-PFP-10 scores between the two groups ($P = 0.71$). There were also no differences between the two groups in the total CS-PFP-10 scores at any of the three follow-up time points (Figure 2 and Table 4). There were also no differences between the two groups in any of the five PFP subscores (upper body strength, upper body flexibility, lower body strength, balance and coordination, and endurance) at any of the three follow-up time points (Table 4). The Five Times Sit to Stand Test, the Timed Up and Go Test, the Berg Balance Test, and 36-item Short Form Health Survey responses were also not different between the intervention and standard-of-care groups at the 1-, 3-, and 6-month time points after study enrollment (*see* online supplement). When we stratified patients by preexisting comorbidities or age tertiles, we found no differences in total

Table 2. Implementation of Physical Therapy Programs

	Intensive PT Patients (*n* = 59)	Standard-of-Care PT Patients (*n* = 61)	*P* Value
Total time in physical therapy, min	408 ± 261	86 ± 63	<0.001
Total number of sessions	12.4 ± 6.5	6.1 ± 3.8	<0.001
ICU sessions	6.4 ± 5.3	3.8 ± 2.4	0.002
Hospital ward sessions	6.2 ± 4.7	3.8 ± 3.0	0.003
Outpatient sessions	3.7 ± 2.8	0	
Average duration of individual sessions, min	39.4 ± 11.0	21.8 ± 3.5	<0.001
ICU sessions	31.3 ± 7.0	21.0 ± 3.2	<0.001
Non-ICU sessions	45.3 ± 13.4	22.0 ± 4.8	<0.001
Number of patients receiving physical therapy by type			<0.001
Respiratory exercises	40	7	
Supine exercises	47	34	
Sitting exercises	49	36	
Standing exercises	43	9	
Functional mobility training	52	49	
Total duration of physical therapy by type, min			
Respiratory exercises	33.8 ± 28.4	10 ± 7.9	<0.001
Supine exercises	88.2 ± 80.1	37.2 ± 31.9	<0.001
Sitting exercises	77.8 ± 52.0	20.3 ± 15.1	<0.001
Standing exercises	74.6 ± 64.2	18.0 ± 13.3	<0.001
Functional mobility training (including gait training)	175.2 ± 121.8	44.5 ± 34.5	<0.001
Total number of physical therapy sessions by location			
ICU	431	222	<0.001
Hospital ward	353	182	<0.001
Outpatient home setting	32	0	<0.001
Outpatient clinic setting	13	0	<0.001

Definition of abbreviations: ICU = intensive care unit; PT = physical therapy.
Data are presented as number or mean ± SD.

Table 3. Intensive Care Unit Medication Duration and Average Daily Dosing

	Intensive PT Patients	Standard-of-Care PT Patients	*P* Value
Benzodiazepines	43	44	
Average number of days	6.0 ± 5.4	6.5 ± 7.4	0.71
Average hourly dose in lorazepam equivalents, mg	0.7 ± 1.1	0.8 ± 1.4	0.81
Propofol	17	15	
Average number of days	3.4 ± 2.9	4.7 ± 2.7	0.21
Average hourly dose, mg	127 ± 110	100 ± 78	0.43
Dexmedetomidine	24	23	
Average number of days	4.0 ± 3.4	4.8 ± 4.4	0.48
Average hourly dose, μg	45 ± 27	53 ± 43	0.43
Opiates	47	49	
Average number of days	7.5 ± 6.9	6.4 ± 7.0	0.44
Average hourly dose in fentanyl equivalents, μg	74 ± 100	82 ± 111	0.70
Neuromuscular blocking agents	7	8	
Average number of days	1.4 ± 0.8	1.0 ± 7.6	0.26

Definition of abbreviation: PT = physical therapy.
Data are presented as number or mean ± SD.

CS-PFP-10 scores at the 1-, 3-, and 6-month time points after study enrollment (*see* online supplement).

The patients who were lost to follow-up were not different from those patients who completed their outpatient assessments. When we compared them with those patients who completed their 3-month assessments, we found that the 23 patients who did not complete their 3-month assessments were not different at baseline in regard to age, Acute Physiology and Chronic Health Evaluation II score, or hospital-free days ($P > 0.05$ for all three analyses).

Overall, 91 PT sessions were stopped early (on average, 0.75 sessions per enrolled patient). The most common reasons were patient fatigue (31%), patient requested to stop for other reasons (21%), patient inability to continue or cooperate with the session (17%), change in patient's vital signs (13%), and other reasons (18%). There was no difference between the two groups in the frequency of stopping a PT session early ($P = 0.79$). There were only two adverse events associated with this clinical trial. One patient had a syncopal episode during a PT session, and another patient was readmitted to the hospital with polyarthralgia that was possibly related to PT interventions.

Discussion

In a cohort of 120 critically ill patients with acute respiratory failure, an intensive PT program did not improve long-term physical functioning compared with a standard-of-care program. There were also no differences between the two study arms in regard to secondary outcomes, including ICU- and hospital-free days. These findings are similar to the results of the only other previous PT intervention trial that included long-term assessments of physical functioning (25). Our study also confirms that patients who survive acute respiratory failure have severe and persistently diminished physical functioning (3, 4). For example, a total CS-PFP-10 score of 57 is an accepted threshold below which the probability of living independently is significantly reduced (47). The average total CS-PFP-10 scores of our patients would predict that the majority would not be able to live independently at 1, 3, and 6 months after hospitalization. These reductions in physical functioning are all the more concerning because of the relatively young age of our patient population and the fact that 100% were living independently at home before hospital admission.

Intensive PT programs for critically ill patients are promising interventions that may improve patient-centered outcomes (48). Potential benefits of early and intensive PT interventions may include improved muscle strength, physical functioning, quality of life, reduced hospital and ICU lengths of stay, shorter duration of mechanical ventilation, and reduced hospital costs (14, 16, 17). On the basis of the results of these primarily observational studies, an ICU culture shift has occurred with a focus on implementing PT interventions (19, 49). Regardless of potential benefits, routine implementation of PT interventions in the ICU remains low (50–52). During the first 14 days of mechanical ventilation, patients from Australian and New Zealand ICUs were observed over a total of 1,288 patient-days (50). Even though these facilities had dedicated PT staffing, PT was performed on only 26% (n = 209) of patient-days. When treatment did occur, the maximum level of exercises occurred in bed (45% of sessions). Our study suggests that the implementation of an intensive PT program may not be indicated for all critically ill patients who require mechanical ventilation for at least 4 days. Much of the rationale for providing intensive PT has been based on shortening ICU and hospital lengths of stay, and therefore on reducing hospital costs (53). Though PT is a relatively safe intervention, it is labor intensive (54). Therefore, studies are needed to identify those patients who may truly benefit from early and intensive PT, so that PT resources can be properly allocated. In addition, enrolling suitable patients who are most likely to benefit from PT would improve the conduct of future clinical trials.

There are several potential reasons for the lack of benefit of our intensive PT program. First, as in most studies of critical care patients, the patient population was fairly heterogeneous. At 1, 3, and 6 months, there was significant variability in the long-term physical function status of our patients. During critical illness, there are multiple causes of acquired weakness and muscle injury. The cellular mechanisms responsible for deconditioning and critical illness polyneuromyopathy are also complex. As a result, there is inherent heterogeneity of patients with ICU-acquired weakness. An intensive PT program that targets specific patients, such as those with weakness due to deconditioning, may yield more positive treatment effects. Future research studies are needed that identify strategies to risk stratify patients for specific types of PT and rehabilitation. Second, the sample size of this study meant that only large improvements could be detected in physical function. Future studies with a larger sample size may be indicated. Third, the duration of our PT program may not have been

Table 4. Physical Functional Performance Test and Other Outcome Measures

	Intensive PT Patients	Standard-of-Care PT Patients	*P* Value
Total CS-PFP-10 scores			
1 mo	19.0 ± 3.7	20.9 ± 4.1	0.73
3 mo	30.7 ± 3.8	36.8 ± 4.3	0.29
6 mo	39.5 ± 3.9	44.0 ± 4.0	0.43
Upper body strength CS-PFP-10 scores			
1 mo	19.5 ± 4.0	22.6 ± 4.6	0.61
3 mo	30.1 ± 4.2	38.5 ± 4.8	0.19
6 mo	40.3 ± 4.5	47.2 ± 4.6	0.29
Upper body flexibility CS-PFP-10 scores			
1 mo	31.8 ± 5.6	30.6 ± 5.5	0.87
3 mo	50.4 ± 5.3	50.1 ± 5.2	0.97
6 mo	61.1 ± 4.3	63.6 ± 4.7	0.69
Lower body strength CS-PFP-10 scores			
1 mo	14.5 ± 3.1	17.6 ± 3.6	0.52
3 mo	23.9 ± 3.4	31.0 ± 4.0	0.18
6 mo	30.4 ± 3.9	36.6 ± 3.8	0.26
Balance and coordination CS-PFP-10 scores			
1 mo	20.7 ± 4.2	20.7 ± 4.0	0.77
3 mo	30.9 ± 3.8	37.2 ± 4.4	0.28
6 mo	40.0 ± 3.9	43.8 ± 4.1	0.51
Endurance CS-PFP-10 scores			
1 mo	19.0 ± 3.7	20.8 ± 4.1	0.74
3 mo	30.8 ± 3.8	37.1 ± 4.4	0.28
6 mo	39.9 ± 3.9	43.9 ± 4.1	0.49
28-d ICU-free days	13 (3–18)	11 (4–18)	0.69
ICU length of stay, d	15 (10–25)	16 (10–24)	0.69
Mechanical ventilation duration, d	10 (7–18)	10 (7–19)	0.89
28-d hospital-free days	7 (0–12)	7 (0–14)	0.97
Hospital length of stay, d	21 (16–32)	21 (14–38)	0.97
Discharged to home	51% (25/49)	49% (27/55)	0.84
90-d institution-free days	61 (39–73)	56 (33–75)	0.87
180-d institution-free days	151 (129–163)	146 (123–165)	0.89

Definition of abbreviations: CS-PFP-10 = Continuous Scale Physical Functional Performance Test short form; ICU = intensive care unit; PT = physical therapy.
CS-PFP-10 scores are presented as mean ± SEM. The CS-PFP-10 total and component scores are scored from 0 to 100, with higher scores indicating better function. Scores vary with age. For adults without disabilities ages 35–54 years, average total CS-PFP-10 scores range from 70.9 to 73.9. Other outcome measures are presented as median (25–75% quartiles).

sufficient to improve physical functioning. Significant limitations in physical function performance persisted in many of the patients 6 months after hospital enrollment. It may be that patients require longer than 1 month of intensive PT. However, patients enrolled in the recent RECOVER trial received prolonged post-ICU interventions and their long-term physical recovery was not improved (55). Fourth, our study intervention was not continued for study patients transferred to another inpatient facility (e.g., long-term acute care, subacute rehabilitation). In the United States, many patients recovering from critical illness are transferred to a long-term acute care facility once they are medically stable (56). Half of the patients in our study were discharged to a location other than home. Physicians and other health-care professionals who care for critically ill patients in acute care hospitals are not commonly involved in determining the PT program after the patient is discharged to a long-term care facility. The success of intensive PT programs may be dependent on better integration with the care received in subsequent facilities. Fifth, we may not have started our intervention early enough. Patients in our study were eligible for enrollment after 4 days of mechanical ventilation and received their first PT session, on average, 8 days after the initiation of mechanical ventilation. In the study by Schweickert and coworkers, patients were eligible for enrollment if they had received mechanical ventilation for less than 3 days (26). Therefore, our patients initiated their PT program at a later time point than the patients in the study by Schweickert and colleagues (26). While the muscles are inflamed and undergoing proteolysis, early PT may potentially be detrimental. The proper time to initiate PT might be best informed through translational studies of muscle injury and repair. Sixth, it is possible that our intervention did not include the most beneficial components of PT. However, our intensive PT program was based upon published models, and overall a higher percentage of our study patients (50%) were discharged to home compared with the Schweickert study (32%) (26). Seventh, our rate of loss to follow-up could have introduced biases that might have affected the conclusions of our study. We did not review a national Social Security database to determine whether some of the loss to follow-up may have been related to death after hospital discharge. However, there does not appear to be significant participation bias, as the 1-month CS-PFP-10 scores were not different between the patients who followed up and those who did not follow up at 3 months. Regardless, there is always concern regarding differential follow-up in long-term outcome studies. We also did not collect information regarding the home or outpatient administration of non–study-related PT to the control subjects. Finally, it is possible that an intensive PT program truly does not yield better physical function than a standard-of-care program.

There are several strengths of this study. First, formal protocols were developed by physical therapists and critical care physicians for both the intensive PT and standard-of-care interventions. Second, the standard-of-care intervention was based upon national survey data of current practices for delivering PT to critically ill patients (39). In addition, all of the sessions were provided by licensed physical therapists who attended formal training sessions before treating any study patients. To maintain treatment fidelity, the first several treatment sessions for each therapist

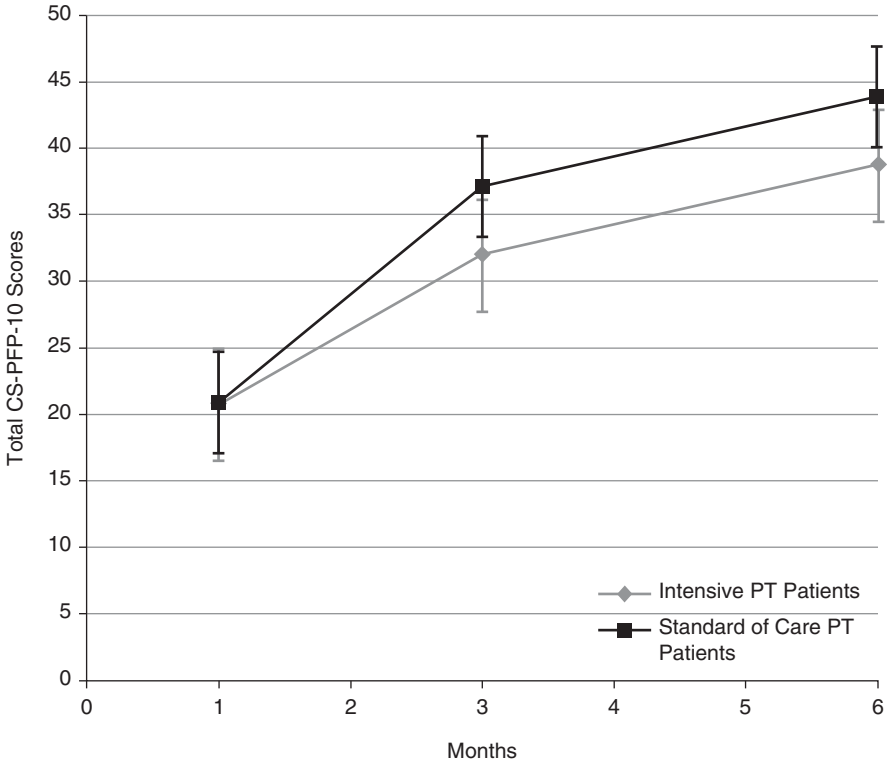

Figure 2. Continuous Scale Physical Functional Performance Test short form (CS-PFP-10) scores in the intensive physical therapy (PT) and standard-of-care PT patients.

were observed by one of the investigators who developed the protocol, and periodic reviews and cotreatment sessions were conducted with study investigators during the trial. Third, the results of the study may be more generalizable as patients were enrolled from both academic and community hospitals. Fourth, there was excellent separation in the amount and intensity of the intervention between the two arms of the study. Fifth, our primary outcome, the CS-PFP-10 score (though labor intensive), is an excellent measure of actual physical performance. Self-report questionnaires measure different constructs than performance-based tests, such as the CS-PFP-10 (57). Schenkman and colleagues determined the CS-PFP-10's reliability and sensitivity to change in subjects who participated in a 12-week exercise program (41). The test–retest reliability of the CS-PFP-10 was 0.93–0.98 for the total score and the individual domains, and the average total CS-PFP-10 score increased by 16.5%. The change for the individual domains ranged from an increase in 20.4% for balance and coordination to 8.1% for upper body flexibility. Finally, this study was conducted with extreme safety, as there were no increased adverse events in patients randomized to the intensive PT intervention group.

In summary, this clinical trial demonstrates that an intensive PT program did not improve long-term physical function performance compared with a standard-of-care PT program. In future studies, researchers should consider determining characteristics that identify patients who require and could benefit from intensive PT, as well as the specific components of PT that are beneficial to patients. On the basis of the long-term limitations in physical function, patients may also require more than a 28-day PT intervention. A larger multicenter trial that considers mortality as a measurable endpoint or a trial that enrolls a select cohort of patients with acute respiratory failure who are more likely to benefit from PT may be indicated to determine the efficacy of these interventions for patients recovering from critical illness. Finally, how occupational and speech therapy are delivered and integrated with PT also needs to be determined. ■

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