The Effect of High Protein and Mobility-Based Rehabilitation on Clinical Outcomes in Survivors of Critical Illness

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BACKGROUND: Protein supplementation and mobility-based rehabilitation programs (MRP) individually improve functional outcomes in survivors of critical illness. We hypothesized that combining MRP therapy with high protein supplementation is associated with greater weaning success from prolonged mechanical ventilation (PMV) and increased discharge home in this population. METHODS: We conducted a retrospective analysis assessing the effects of an MRP on a cohort of survivors of critical illness. All received usual care (UC) rehabilitation. The MRP group received 3 additional MRP sessions each week for a maximum of 8 weeks. Subjects were prescribed nutrition and classified as receiving high protein (HPRO) or low protein (LPRO), based on a recommended 1.0 g/kg/d, and then the subjects were categorized into 4 groups: MRP+HPRO, MRP+LPRO, UC+HPRO, and UC+LPRO. RESULTS: A total of 32 subjects were enrolled. The MRP+HPRO group had greater weaning success (90% vs 38%, *P* = .045) and a higher rate of discharge home (70% vs 13%, *P* = .037) compared to UC+LPRO group. The MRP+HPRO group had a higher, nonsignificant rate of discharge home compared to the MRP+LPRO (70% vs 20%, *P* = .10). CONCLUSIONS: Combining high protein with mobility-based rehabilitation was associated with increased rates of discharge home and ventilator weaning success in survivors of critical illness. Further studies are needed to evaluate the role of combined exercise and nutrition interventions in this population. *Key words: rehabilitation; nutrition therapy; mechanical ventilation; weaning; critical illness; patient discharge.* [Respir Care 2021;66(1):73–78. © 2021 Daedalus Enterprises]

Introduction

Survivors of critical illness represent a unique patient population at high risk for adverse outcomes, including the loss of functional independence resulting in decreased quality of life.[1-3] Many survivors of critical illness suffer from ICU-acquired weakness and require prolonged mechanical ventilation (PMV), often resulting in admission to long-term acute care hospitals (LTACH) for ventilator weaning. Up to 10% percent of acutely ill patients requiring mechanical ventilation ultimately develop chronic critical illness.[4] Of these patients, < 12% are both alive and independent at 1 y after their acute illness.[4]

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Two major factors affecting outcomes in survivors of critical illness are malnutrition and physical deconditioning.[4,5] Both nutritional supplementation and physical exercise, often in the form of mobility-based rehabilitation programs (MRP), have been proposed as methods to improve functional outcomes in critically ill patients.[6-9] Additionally, protein supplementation combined with resistance exercise has been shown to increase lean body mass in frail elderly patients.[10] However, a Cochrane review of the use of protein and energy supplements in elderly subjects at risk for malnutrition reported no evidence that supplements reduced hospital stay or led to improvements in function.[11] Despite a modest body of knowledge describing nutrition interventions on ICU survivors, less is known about the effects of these interventions in the chronically critically ill population, such as patients with ICU-acquired weakness requiring PMV. In a previous study, we reported that an MRP resulted in greater success at weaning from PMV and higher rates of discharge home compared to usual care (UC) in a group of survivors of critical illness requiring PMV.[12] However, the nutritional status of subjects in that study was not considered to be a factor affecting the outcome of this cohort.

Nutritional optimization, high protein supplementation in particular, improves outcomes in the critically ill and post-ICU populations. We hypothesized that the combined therapy of an MRP with high protein supplementation would be associated with greater success at weaning from PMV and higher rates of discharge home in survivors of critical illness. To test this hypothesis, we performed a retrospective, post hoc analysis of a pilot study that randomized survivors of critical illness with ICU-acquired weakness receiving PMV to either UC or UC with MRP. We then evaluated their nutritional status to determine whether the combination of high protein and exercise had an effect on outcomes in this population.

QUICK LOOK

Current knowledge

Survivors of critical illness often suffer from ICU-acquired weakness and require prolonged mechanical ventilation, often resulting in admission to long-term acute care hospitals for ventilator weaning. Both nutritional supplementation and mobility-based rehabilitation programs improve functional outcomes in critically ill patients.

What this paper contributes to our knowledge

The combination of high protein with mobility-based rehabilitation is associated with increased rates of discharge home and ventilator weaning success in survivors of critical illness. This study highlights the need for further investigation into nutritional supplementation in survivors of critical illness enrolled in exercise rehabilitation programs.

Methods

This was a retrospective, post hoc analysis of a pilot study of older subjects with ICU-acquired weakness discharged from an ICU to an LTACH for rehabilitation, ventilator weaning, and continued medical care.[12] Middle-aged and older patients receiving PMV were screened for ICU-acquired weakness on admission to the LTACH. Eligibility criteria included those age $\geq$ 50 y with tracheostomy on PMV for at least 14 d during acute hospitalization and requiring PMV for $\geq$ 6 h/d, able to participate in MRP activities with preadmission Barthel Index $>$ 70, with all extremities intact and mobile, and meeting clinical criteria for ICU-acquired weakness. We excluded patients with acute superimposed cardiopulmonary disease, cognitive impairment, or severe functional impairment related to neuromuscular dysfunction. Those who met eligibility criteria and provided informed consent underwent baseline functional assessments and were randomized to receive either UC or UC with MRP. Subjects received serial functional assessments every 2 weeks, which consisted of validated functional measures and bedside assessment of basic functional mobility.

The MRP was a standardized, patient-specific rehabilitation program based upon each individual's functional level (ie, bed-dependent, chair-dependent, or ambulatory). The MRP combined muscle strengthening and endurance, aerobic conditioning, and functional mobility activities with the goal to progress the patient to the next higher level of function and mobility. MRP sessions were administered for 45–60 min, 3 times per week, separate from the other UC physical therapy sessions conducted at the LTACH. Of note, subjects were provided supplemental oxygen or ventilator support during MRP sessions to meet their respiratory needs at a level equivalent to the highest settings required over the 3 d prior to the physical therapy session.

For the bed-dependent group, the MRP focused on manually resistive functional exercises and assisted functional activities. Subjects who were able to transfer to a chair with minimal assistance were considered chair-dependent. The chair-dependent MRP focused on pre-walking activities, progression of aerobic training, and standing transfers and balances. Subjects were considered ambulatory when they were able to walk with minimal assistance for $\geq$ 25 feet. The MRP for ambulatory subjects focused on higher levels of muscle endurance training, pre-stair climbing, and dynamic standing activities.

UC was defined by a retrospective review of 20 patient charts and 5 observations of physical therapy sessions of patients at our university-based LTACH. Muscles were exercised in isolation using basic therapeutic activities not associated with a specific functional task. Ten repetitions of each exercise were generally completed, without targeting any particular goal in regard to training effect or physiologic response. These sessions were scheduled up to 3 times weekly but were missed about 25% of the time due to diagnostic testing, procedures, or lack of patient motivation.

All patients were assessed by a registered dietitian upon admission to an LTACH. They were prescribed nutrition based on estimated energy needs, per standard of care. The prescribed nutrition, specifically daily protein recommendations, was reviewed. We chose the median recommendation of 1.0 g/kg/d of protein as the discriminator value in classifying subjects as receiving high protein (HPRO) or low protein (LPRO) intake. Of note, 1.0 g/kg/d of protein was slightly higher than the recommended maintenance dose for active, older community dwellers, but not as high as the recommended protein dose (1.2–2.0 g/kg/d) for acutely critically ill patients.[13] We classified subjects as receiving HPRO or LPRO intake based on this median recommendation. Subjects were thus categorized into 4 groups: MRP with high protein (MRP+HPRO), MRP with low protein (MRP+LPRO), UC with high protein (UC+HPRO), and UC with low protein (UC+LPRO).

Data were expressed as mean ± SD or counts (*n*) with percentages. The chi-square test was used to compare the proportion of subjects successfully weaned and discharge disposition among patients in the 4 different groups; a P value $\leq .05$ indicated statistical significance. We defined successful weaning from PMV as the ability to tolerate tracheostomy collar for at least 48 h without requiring mechanical ventilator support, or 7 consecutive days requiring only nocturnal ventilation for ≤ 8 h. Subjects discharged from the LTACH without being weaned from PMV were assigned 56 ventilator days, which corresponded to the maximum length of follow-up of 8 weeks.

Results

A total of 32 subjects were enrolled in the study from August 2013 to December 2014 (Fig. 1). One subject was enrolled but withdrew before baseline testing and randomization. Of the remaining 31 subjects, 15 were randomized to MRP and 16 were randomized to UC. One subject in the group randomized to receive UC was excluded due to incomplete nutrition data. Subjects were 55% male with an average body mass index of 32.2 ± 11.5 kg/m^2 and mean age of 60 ± 12 y. There were no significant differences between baseline characteristics regarding age, gender, race, Barthel Index, or Charlson Comorbidity Index. However, there was a statistically significant difference in body mass index between the LPRO and the HPRO groups. Both LPRO groups had a higher mean body mass index of 39.0 ± 12.1 kg/m^2 (UC+LPRO) and 46.5 ± 11.9 kg/m^2 (MRP+LPRO) compared to 24.5 ± 6.8 kg/m^2 (UC+HPRO) and 25.6 ± 7.0 kg/m^2 (MRP+HPRO) (Table 1).

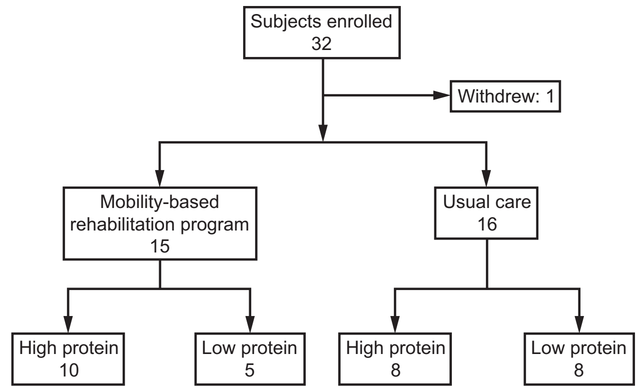

Fig. 1. Flow chart.

Compared to UC+LPRO (3 of 8 subjects), MRP+HPRO (9 of 10 subjects) had greater weaning success from PMV (38% vs 90%, $P = .045$) (Table 2). There was no statistically significant difference between the MRP+HPRO group and the MRP+LPRO group regarding ventilator weaning. There was also no difference between UC groups receiving high versus low protein in regard to ventilator weaning.

More subjects were successfully discharged home in MRP+HPRO (7 of 10 subjects) compared to UC+LPRO (1 of 8 subjects), and this difference was statistically significant (70% vs 13%, $P = .037$) (Table 2). Although not statistically significant, there was a notable difference in discharge status between MRP+HPRO (7 of 10 subjects) compared to MRP+LPRO (1 of 5 subjects, or 70% vs 20%, $P = .10$). There was no significant difference between UC+HPRO (1 of 8 subjects) versus UC+LPRO (1 of 8 subjects) regarding discharge status (13% vs 13%, $P > .99$).

Discussion

Our study suggests that the combination of protein and exercise is associated with greater success in weaning from PMV and higher rates of discharge home from an LTACH among survivors of critical illness compared to those who received MRP only and UC regardless of protein intake. There was no significant difference in outcomes between HPRO and LPRO intake alone, but the significant difference in weaning and discharge status between UC versus MRP highlights what previous studies have shown regarding the benefits of exercise and physical rehabilitation in regard to functional outcomes in critical illness.[12,14,15] This study demonstrates that these interventions can be applied

Table 1. Baseline Demographic Characteristics

Characteristic	MRP+HPRO	MRP+LPRO	UC+HPRO	UC+LPRO	*P*
Subjects, *n*	10	5	8	8	NA
Age, y	57.8 ± 12.2	55.8 ± 12.8	67.4 ± 10.5	58.9 ± 12.1	.27
Male	6 (19.4)	2 (6.5)	5 (16.1)	4 (12.9)	.85
Race					.96
African American	6 (19.4)	3 (9.7)	4 (12.9)	4 (12.9)	
White	4 (12.9)	2 (6.5)	4 (12.9)	4 (12.9)	
Body mass index, kg/m^2	25.6 ± 7.0	46.5 ± 11.9	24.5 ± 6.8	39.0 ± 12.1	< .001
Barthel Index	99.0 ± 2.1	91.0 ± 12.4	91.1 ± 13.9	91.3 ± 6.6	.45
Charlson Comorbidity Index	4.7 ± 3.2	4.0 ± 2.5	4.5 ± 2.4	4.4 ± 1.7	.97
Albumin	3.0 ± 0.9	3.2 ± 0.6	3.0 ± 0.6	2.7 ± 0.6*	.63
Physical therapy sessions, no.	29.0 ± 19.3	21.0 ± 14.1	14.7 ± 15.3*	13.9 ± 9.8	.17

Data are presented as mean ± SD or *n* (%).
* *n* = 7; one subject was excluded due to incomplete data.
MRP = mobility-based rehabilitation program; UC = usual care; HPRO = high protein; LPRO = low protein; NA = not applicable.

Table 2. Comparison of Wean Status and Discharge Home Among Different Groups

Groups Compared		Subjects, *n*	Weaned	*P*	Discharge Home	*P*
1	MRP+HPRO	10	9 (90)	.045	7 (70)	.037
	UC+LPRO	8	3 (38)		1 (13)	
2	MRP+HPRO	10	9 (90)	.60	7 (70)	.10
	MRP+LPRO	5	4 (80)		1 (20)	
3	MRP+HPRO	10	9 (90)	.045	7 (70)	.037
	UC+HPRO	8	3 (38)		1 (13)	
4	MRP+LPRO	5	4 (80)	.21	1 (20)	.73
	UC+HPRO	8	3 (38)		1 (13)	
5	UC+HPRO	8	3 (38)	> .99	1 (13)	> .99
	UC+LPRO	8	3 (38)		1 (13)	
6	MRP+LPRO	5	4 (80)	.21	1 (20)	.73
	UC+LPRO	8	3 (38)		1 (13)	

Data are presented as *n* (%).
MRP = mobility-based rehabilitation program; UC = usual care; HPRO = high protein; LPRO = low protein.

to survivors of critical illness requiring PMV with similar results in improved functional outcomes.

One of the goals of adequate nutrition delivery, protein in particular, in critically ill patients is to attenuate acute skeletal muscle wasting, which is a significant contributor to ICU-acquired weakness.[16] Many studies to date have investigated the effects of improved nutrition or high protein intake on functional outcomes and acute skeletal muscle wasting in critically ill subjects. In the EDEN trial, 1,000 subjects with acute lung injury were randomized to receive either trophic or full enteral feeding for the first 6 d and in their post hoc analysis, more subjects in the full-feeding group were more likely to be discharged home.[17] Elke et al[18] performed a secondary analysis of ICU subjects on enteral nutrition and found that an increase of 30 g of protein per day (from a mean amount of 0.7 g/kg/d) was associated with more ventilator-free days and reduced mortality at 60 d. Ferrie et al[19] randomized 119 subjects to receive 0.8 or 1.2 g/kg protein via parenteral nutrition; although there was no difference in handgrip strength at ICU discharge, there was a significant difference in secondary outcomes, such as increased handgrip strength at day 7, greater forearm muscle thickness, and decreased fatigue scores in the higher protein group.

Our study is one of the first studies to examine the effects of protein supplementation on functional outcomes in survivors of critical illness in an LTACH. The majority of studies and ongoing trials assess the effects of exercise and nutrition in critically ill subjects in acute care settings, rather than in long-term acute or chronic care facilities. Another area of increasing interest is the role of exercise rehabilitation programs to improve strength, functional outcomes, and long-term quality of life in survivors of critical illness.[6,9] However, there is a paucity of evidence regarding nutritional supplementation in this population, highlighting the need for further investigation, both individually and when combined with exercise.

One of the challenges that we encountered was formulating an appropriate protein prescription based on body mass index. We found a statistically significant difference between the HPRO group and the LPRO group with regard to body mass index, with the LPRO group having a significantly higher mean body mass index. This is based on prescribed diet by the registered dietitian, which is generally based on American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines.[13] Recommendations for patients of normal weight are based on actual body weight. In obese patients, ASPEN guidelines recommend high-protein, hypocaloric feeds for critically ill patients,[20] with actual protein prescriptions based on ideal rather than actual body weight. Thus, these guidelines have not completely gained universal acceptance in practice because the recommended protein per kilogram body weight for an obese patient will be much lower than that for a patient of normal weight, resulting in apparent undernutrition of obese patients.[21]

One of the limitations to this study is that this was a retrospective post hoc analysis of a pilot study, which limited our data collection to preexisting variables recorded and entered into the electronic medical record by nursing and other ancillary staff. Because we were not physically present to observe the actual nutrition intake of each subject, we conducted our data collection under the assumption that the data in the electronic medical record were accurate. Therefore, we decided to use the initial dietary prescription ordered by the registered dietitian. We cannot evaluate whether the subject actually received the nutrition prescribed. However, based on other large studies,[13,22] inpatients generally receive about 65–70% of their prescribed daily nutrition, and we do not expect a difference in protein or caloric delivery between those in the HPRO group and those in the LPRO group. Additionally, the sample size of this study was too small to do a subgroup analysis of subjects according to body weight, but an area of interest for future study is to evaluate whether there is a difference in outcomes in obese chronically critically ill patients versus normal weight individuals in regard to ventilator weaning and successful discharge home. Lastly, this was a post hoc analysis of a prior pilot study, so a power analysis was not performed. We acknowledge that these results are primarily hypothesis-generating pilot study data, from which future investigations can be planned.

Conclusions

Our study results indicate that the combination of high protein supplementation and an MRP is associated with greater success at weaning from PMV and higher rates of discharge home in subjects with ICU-acquired weakness treated in an LTACH. These preliminary findings support the theory that such a combined intervention may have an additive, beneficial role in improving clinical outcomes of debilitated, mechanically ventilated survivors of critical illness.

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