


Early Physical Rehabilitation in the ICU: A Review for the Neurohospitalist

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**Pedro A. Mendez-Tellez, MD¹, Rasha Nusr, MBBS, MPH²,
Dorianne Feldman, MD, MSPT³, and Dale M. Needham, MD, PhD^{2,3}**

Abstract

Advances in critical care have resulted in improved intensive care unit (ICU) mortality. However, improved ICU survival has resulted in a growing number of ICU survivors living with long-term sequelae of critical illness, such as impaired physical function and quality of life (QOL). In addition to critical illness, prolonged bed rest and immobility may lead to severe physical deconditioning and loss of muscle mass and muscle weakness. ICU-acquired weakness is associated with increased duration of mechanical ventilation and weaning, longer ICU and hospital stay, and increased mortality. These physical impairments may last for years after ICU discharge. Early Physical Medicine and Rehabilitation (PM&R) interventions in the ICU may attenuate or prevent the weakness and physical impairments occurring during critical illness. This article reviews the evidence regarding safety, feasibility, barriers, and benefits of early PM&R interventions in ICU patients and discusses the limited existing data on early PM&R in the neurological ICU and future directions for early PM&R in the ICU.

Keywords

bed rest, deconditioning, early ICU rehabilitation, early Neuro-ICU rehabilitation, feasibility, immobility, muscle weakness, outcomes, safety

Introduction

Advances in critical care have resulted in improved intensive care unit (ICU) mortality. As a consequence, there are a growing number of ICU survivors living with long-term sequelae of critical illness, such as impaired physical function and quality of life (QOL).

In addition to critical illness, prolonged bed rest and immobility in the ICU lead to a loss of muscle mass and muscle weakness. Intensive care unit-acquired weakness (ICUAW) may occur in 25% of patients requiring mechanical ventilation for >1 week¹ and is associated with increased duration of mechanical ventilation and weaning,²⁻⁵ longer ICU and hospital stay,^{2,3} and increased mortality.⁶⁻⁸ Impairments in physical function and exercise capacity may last for years after ICU discharge.⁹ Thus, there is a need for interventions that may attenuate or prevent weakness and physical impairments occurring during critical illness.

This article first reviews the etiology, risk factors, and long-term sequelae of muscle weakness in the ICU as well as the clinical features of ICUAW and a diagnostic approach. We then discuss the role of early Physical Medicine and Rehabilitation (PM&R) interventions in the ICU to address these physical sequelae, including evidence regarding its safety, feasibility, barriers, and benefits. This article

concludes by discussing the limited existing data on early PM&R in the neurological ICU and future directions for early PM&R in the ICU.

ICU-Acquired Weakness

Muscle weakness and physical impairments after critical illness may be due to (1) a preexisting neuromuscular disorder, such as myasthenia gravis, (2) a new neurological disease causing the need for ICU admission, such as Guillain-Barré syndrome, (3) a complication of critical illness (ICUAW), or (4) post-ICU mood changes or persistent pain that may affect survivors' capacity or willingness to perform physical

¹ Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

² Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

³ Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Corresponding Author:

Pedro A. Mendez-Tellez, Department of Anesthesiology and Critical Care Medicine, 600 North Wolfe Street, Baltimore, MD 21287, USA
Email: pmendez@jhmi.edu

activities.¹⁰ ICU-acquired weakness refers to the acute onset of diffuse, symmetric, generalized muscle weakness that develops after the onset of critical illness without other identifiable cause.¹¹

Etiology and Risk Factors Associated With Muscle Weakness After Critical Illness

The etiology of ICUAW is multifactorial and may include (1) prolonged bed rest and immobility leading to deconditioning and disuse atrophy, (2) critical illness polyneuropathy (CIP), critical illness myopathy (CIM), or a combination of these conditions, known as critical illness neuromyopathy (CINM), or (3) prolonged neuromuscular blockade.¹¹ Commonly cited risk factors for ICUAW and CINM include the systemic inflammatory response syndrome, sepsis, and multiple organ dysfunction syndrome (MODS); hyperglycemia; and medications, such as corticosteroids and neuromuscular blocking agents (NMBAs).⁸

Bed rest and immobilization. Prolonged bed rest leads to decreased protein synthesis, enhanced proteolysis, and a net loss in the muscle mass and muscle strength.¹² In healthy, well-nourished volunteers, there is a 4% to 5% loss of muscle strength for each week of bed rest.¹³ In critically ill patients, the onset of muscle atrophy is rapid and severe, beginning within days of hospitalization.¹⁴ Both oxidative stress and proinflammatory cytokines have been investigated as potential causes for myopathy during critical illness. Limited data suggest that prolonged inactivity contributes to imbalances in the inflammatory response with increased proinflammatory cytokine and oxidative stress activity.^{15,16} In 3 studies, the duration of mechanical ventilation, as a potential surrogate measure of bed rest and immobility, was associated with ICUAW.^{1,17,18}

Systemic inflammatory response, sepsis, and MODS. The systemic inflammatory response and MODS have been associated with the loss of muscle mass¹⁹ and neuromuscular abnormalities.^{2,20} Clinically detectable muscle weakness has been associated with the number of days with organ dysfunction in 2 or more systems and the number of days receiving vasoactive drugs.¹⁷ These neuromuscular abnormalities are regarded as part of sepsis-associated MODS.²¹

Hyperglycemia. Hyperglycemia is an identified risk factor for neuromuscular abnormalities. Two large randomized controlled trials of intensive insulin therapy for tight glycemic control (blood glucose target 80-110 mg/dL) demonstrated a strong association between hyperglycemia and the presence of abundant spontaneous electrical activity with needle electromyography (EMG); however, no clinical evaluation of muscle strength was performed to supplement this limited EMG evaluation.^{22,23}

NMBAs and corticosteroids. Controversy exists regarding the associations of NMBAs and/or use of corticosteroids with ICUAW. For instance 2 prospective studies, which adjusted for potential confounders, found a significant independent association of NMBAs with ICUAW^{2,24} whereas in other studies NMBAs were not associated with ICUAW.²⁵ Similarly, a prospective cohort study demonstrated a significant independent association of corticosteroids with ICUAW but could not detect an association with dose or duration of corticosteroid therapy. However, other prospective studies could not identify corticosteroids as an independent factor for CINM.^{2,17,20,26} Conversely, 1 trial of intensive insulin therapy reported that corticosteroids had a protective effect against the presence of EMG abnormalities in critically ill patients receiving intensive insulin therapy.²⁴

Clinical Presentation and Evaluation

Critically ill patients who demonstrate clinically evident weakness and/or prolonged ventilator dependence should be evaluated for ICUAW. Physical findings show diffuse symmetric weakness and decreased tone. Deep tendon reflexes may be normal, reduced, or absent.¹¹ Table 1 provides a comparison of the clinical, electrophysiological, and pathological features of common ICU neuromuscular abnormalities.

Electrophysiological studies. Electromyography (EMG) and nerve conduction studies (NCSs) can help identify abnormalities in sedated or uncooperative patients who cannot be clinically examined for muscle strength. Electrophysiological abnormalities are present early and precede clinical manifestations of muscle weakness.²⁸ Typically, CIP is characterized by a sensorimotor axonopathy with markedly reduced compound muscle action potentials (CMAPs) and sensory nerve action potentials (SNAPs), whereas nerve conduction velocities and distal latencies are minimally affected.²⁹ Needle EMG demonstrates abnormal spontaneous activity with fibrillation potentials and positive sharp waves.^{29,30} Typical features of CIM include low-amplitude, sometimes broadened or absent, CMAPs and relatively preserved SNAPs,³¹ and needle EMG demonstrates low amplitude, short duration, and polyphasic motor unit action potentials, with good recruitment pattern despite the pronounced weakness.³² Fibrillation potentials and positive sharp potentials, which are usually indicative of axonal injury, may also occur in CIM (PM-T).³² Routine EMG/NCS may be unable to discriminate between CIP and CIM in unconscious, uncooperative, or extremely weak patients without additional testing, such as direct muscle stimulation.^{33,34} Participants with CIM demonstrate reduced or absent direct muscle excitability.³⁵ Electrophysiological studies require resources and expertise and therefore are not universally available in all ICUs. Moreover, it is currently unclear whether all abnormal EMG/NCS findings have clinical importance to patients.¹¹

Table 1. Features of Neuromuscular Abnormalities of Critical Illness^a

	Critical Illness Polyneuropathy	Critical Illness Myopathy	Disuse Atrophy
Setting	Sepsis, SIRS, MODS	Most common with NMBAs, steroids, asthma, organ transplant	Prolonged bed rest/immobility Prolonged sedation
Clinical features	Generalized or distal muscle weakness Cranial nerves usually spared Distal sensory deficit Preserved or depressed DTRs	Generalized or predominantly proximal muscle weakness No sensory impairment Preserved or depressed DTRs Elevated CK levels: 10- to 100-fold	Muscle wasting with flaccid weakness Normal or reduced strength with marked diminished endurance No sensory deficits Preserved DTRs
Nerve conduction studies	CMAP decreased to <80% of LLN in ≥ 2 nerves SNAP decreased to <80% of LLN in ≥ 2 nerves Normal conduction velocity	CMAP decreased to <80% of LLN in ≥ 2 nerves SNAPs are >80% of LLN in ≥ 2 nerves NCVs normal or near-normal without conduction block	Normal NCS, or Modest decreased CMAP with preserved SNAP
Needle EMG	Abnormal spontaneous activity Large polyphasic MUAPs Reduced recruitment/interference pattern	Variable spontaneous activity Small polyphasic MUAPs in ≥ 2 muscle groups, Low-amplitude, full interference pattern	Abnormal/absence of spontaneous activity Polyphasic MUAP
Direct muscle stimulation	Reduced ne-CMAP Normal dm-CMAP ne-CMAP to dm-CMAP ratio <0.5 ³²	Reduced ne-CMAP and dm-CMAP ne-CMAP: dm-CMAP ratio > 0.5 in ≥ 2 muscle groups	
Biopsy	Axonal degeneration of motor and sensory nerve fibers	Thick filament (myosin) loss Necrotizing myopathy Inflammatory infiltrate may be present	Shift from slow twitch (type I) to fast twitch (type II) muscle fibers Decreased muscle fiber size Little or no inflammatory infiltrates

^a Modified from Stevens R¹¹ and Fan E.²⁷

Abbreviations: CK, serum creatine kinases; CMAP, compound muscle action potential; dm-CMAP, direct muscle stimulated muscle action potential; DTRs, deep tendon reflexes; LLN, lower limit of normal; MODS, multiple organ dysfunction; MUAP, motor-unit action potential; ne-CMAP, nerve stimulated compound muscle action potential; NMBAs, neuromuscular blocking agents; NCVs, nerve conduction velocities; SIRS, systemic inflammatory response syndrome; SNAP, sensory nerve action potential.

Muscle and nerve biopsy. Histological studies have contributed substantially to our understanding of neuromuscular impairments in critical illness. In patients with CIP, nerve biopsy demonstrates an axonal degeneration of motor and sensory nerve fibers,³⁶ resulting in extensive denervation atrophy of limb and respiratory muscles.³⁷ Muscle biopsies have demonstrated 3 morphologic subtypes of ICU-acquired myopathies. Thick filament myopathy is characterized by selective proteolysis and loss of myosin filaments. Acute necrotizing myopathy is characterized by muscle fiber vacuolization and phagocytosis of myocytes. In cachectic myopathy, the muscle fibers show caliber variations, angulations, internalized nuclei, rimmed vacuoles, fatty degeneration, and fibrosis.³⁷ A biopsy may be helpful to help determine an etiology or pathological process when specific diagnostic information is required for clinical care.

Diagnostic Strategy

The diagnosis of ICUAW is based on clinical presentation, predisposing factors, and clinically detectable muscle

weakness, on physical examination, in a critically ill patient in whom there is no plausible etiology other than critical illness. Given the challenges of EMG/NCS in the ICU, EMG/NCS are generally conducted in patients for whom an alternative cause of muscle weakness is being considered, particularly in patients with unexpected severe muscle weakness or slow recovery. These tests may be sometimes performed in patients who cannot have a complete physical examination or are having difficulties with weaning from mechanical ventilation.

Outcomes of Patients With ICUAW

ICU-acquired weakness is independently predictive of poor patient outcomes. Liberation from mechanical ventilation may be 2 to 7 times longer²⁻⁴ with prolonged ICU and hospital stays.^{2,3} Furthermore, clinically detectable ICUAW at the time of awakening has been independently associated with increased hospital mortality in 2 studies.^{6,7} Clinical evidence of recovery of muscle strength may occur within weeks in mild cases and within months in severe cases of ICUAW. In



Figure 1. The feasibility of early ambulation is illustrated in this 56-year-old man admitted to The Johns Hopkins Medical Intensive Care Unit with respiratory and renal failure. The patient is being ambulated while on mechanical ventilation, with the assistance of a physical therapist, respiratory therapist, nurse, and a physical therapy technician. Additional equipment included a portable ventilator, a portable cardiac monitor, a wheeled pole with intravenous infusion pumps, and a wheeled walker. A wheelchair is being pushed behind the patient by a physical therapy technician (not seen). Reprinted with permission from Needham et al.⁴⁶

1 study, the median duration of ICUAW after awakening was 21 days, with 94% of the ICU survivors having a meaningful clinical recovery by 9 months.¹ In more severe cases, however, recovery is incomplete or does not occur at all. Persistent muscle weakness and electrophysiological abnormalities have been reported up to 5 years after ICU discharge.³⁸ Survivors of severe critical illness frequently report persistent functional limitations and impaired QOL for months and years after ICU, which they attribute to neuromuscular issues, including muscle wasting and weakness and residual motor and sensory deficits.^{9,39}

Strategies for Prevention and Treatment of ICUAW

While there is growing knowledge about the epidemiology and mechanisms of ICUAW, to date there are few options for its prevention and/or treatment.⁴⁰ Timely and intensive treatment of sepsis and MODS are key to critical care medicine and may help reduce neuromuscular abnormalities. Although tight glycemic control with intensive insulin therapy may decrease the incidence of electrophysiological neuromuscular abnormalities, in large multicenter studies, this intervention has been associated with an increased risk of hypoglycemia

and in-hospital death.⁴¹ Avoidance of corticosteroids and/or NMBAs, where possible, may be prudent until future studies can clarify their role in ICUAW. The next section of this article will discuss the role of early PM&R interventions for improving ICUAW and physical function.

PM&R in the ICU

Early PM&R in the ICU refers to all physical therapy (PT), occupational therapy (OT), and other rehabilitation activities initiated immediately upon achieving physiologic stability and continued throughout the ICU stay. Such activities may start within 1 or 2 days of initiation of mechanical ventilation. During PM&R activities, patients may still require mechanical ventilation, vasopressors, and dialysis. The goal of early PM&R is to prevent or attenuate neuromuscular complications arising from immobility and prolonged bed rest.

Feasibility

ICU patients are frequently perceived as “too ill” to participate in early PM&R therapies.⁴² However, trials have shown that early PM&R activities are feasible within 24 to 48 hours of initiation of mechanical ventilation.^{43,44} In a large case series of 103 patients, 41% of all mobilization events occurred in intubated patients, with ambulation occurring in 42% of these events.⁴⁵ In addition, a prospective trial of 280 medical ICU patients requiring mechanical ventilation on admission was successful in using a dedicated mobility team to initiate physical therapy within 48 hours of admission. This trial demonstrated that many more patients assigned to the mobility team (vs usual care) received physical therapy in the ICU (73% vs 6%, $P < .001$).⁴⁴ Figure 1 illustrates the feasibility of early mobilization of mechanically ventilated patients.

Safety

In experienced ICUs, early PM&R interventions are safe, even for mechanically ventilated patients. One study with prospective monitoring of safety events reported an event rate of <1% in 1449 activity events. None of these safety events resulted in extubation, additional therapy, higher cost, or longer hospital stay.⁴⁵ Another trial reported no adverse events among 114 patients who received early PT in the ICU.⁴⁴ Safety of early PM&R is aided by careful patient screening and trained staff who carefully evaluate patients’ physiological changes during graduated interventions.⁴⁷ Figure 2 provides an example screening algorithm for active rehabilitation therapy for ICU patients.

Benefits

Early PM&R has been consistently associated with improvement in patients’ mobility and physical function. In a large case series⁴⁵ of 89 ICU survivors, 69% were able to ambulate >100 feet at the time of ICU discharge. Moreover, a

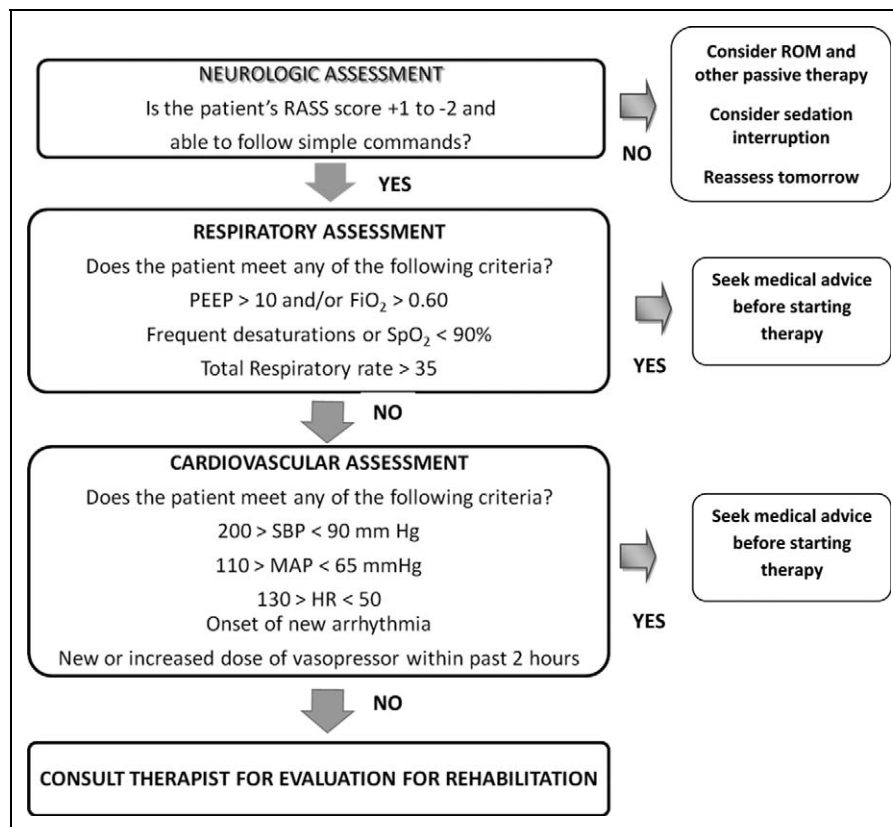


Figure 2. Screening algorithm to evaluate for appropriateness for PM&R activity. FiO_2 indicates fractional of inspired oxygen; HR, heart rate; MAP, mean arterial pressure; PEEP, positive end-expiratory pressure; RASS, Richmond Agitation Sedation Scale; ROM, range of motion; SBP, systolic blood pressure; SpO_2 , saturation of peripheral oxygen. Modified from Korupolu et al.⁴⁷

nonrandomized trial demonstrated that mechanically ventilated patients that received early PT (vs usual care) were out of bed earlier (5 vs 11 days, $P = <.001$).⁴⁴

The strongest evidence for benefit of early PM&R comes from a 2-site, randomized controlled trial of 104 mechanically ventilated patients receiving very early PT and OT started at the beginning of respiratory failure.⁴⁸ Both the intervention and usual care groups received daily sedation interruption and daily spontaneous breathing trials. Participants in the intervention group received progressive mobilization and activities of daily living interventions started at 1.5 days after intubation (vs 7.3 days in the usual care group, $P = <.01$). This trial demonstrated that early intervention led to better outcomes at hospital discharge, including return to independent function (59% vs 35%, $P = .02$), physical function (median Barthel Index 75 vs 55, $P = .05$), and ventilator-free days (median 23.5 vs 21.1, $P = .05$).⁴⁸

Early PM&R is also associated with shorter ICU and hospital stays and potentially improved outcomes after hospital discharge. In a nonrandomized trial of an early mobility team, there was a shorter adjusted mean ICU and hospital length of stay ([LOS]; 5.5 vs 6.9 days, $P = .025$ and 11.2 vs 14.5 days, $P = .006$, respectively)⁴⁴ and a significantly greater odds of surviving without hospital readmissions during

1-year follow-up (odds ratio 1.77, $P = .0362$).⁴⁹ In addition, a quality improvement project with before–after comparison demonstrated that intensive PT and OT in mechanically ventilated MICU patients was associated with a 30% and 18% decrease in ICU and hospital LOS, respectively, and a 20% increase in ICU admissions.⁴⁶

Perceived Barriers

There are potential perceived barriers to implementing early PM&R in ICU patients. Commonly perceived patient-related barriers include delirium, cardiopulmonary instability, and obesity. Both ICU- and institution-related barriers include sedation practices, safety concerns, local beliefs and attitudes, and lack of staffing or expertise.⁵⁰ In particular, sedation substantially reduces patients' ability to engage in active PM&R activities and prolongs the duration of mechanical ventilation and ICU and hospital LOS.^{45,46,51} In many ICUs, it is a customary for mechanically ventilated patients to be deeply sedated and immobile.^{52,53} However, existing studies evaluating early PM&R in the ICU consistently demonstrate that deep sedation is not necessary for the comfort and safety of mechanically ventilated patients, even when ventilated via an oral endotracheal tube.^{49,54} Trained staff and a supportive

ICU culture are important for successfully introducing early PM&R. One study of mechanically ventilated patients noted that the odds of ambulation were 2.5 greater after transfer to an ICU in which early mobilization was a priority.⁵¹ This increase in ambulation could not be accounted for by differences in patients' severity of illness, suggesting that many ICU patients are subjected to unnecessary immobilization due to the routine care practices and culture of the ICU.

Implementing an Early ICU Physical Medicine and Rehabilitation Program

Initiating an early ICU PM&R program requires a multifaceted approach which includes (1) assembling a multidisciplinary team of physicians, nursing, and respiratory, physical, and occupational therapists, (2) identifying local barriers to PM&R implementation, and (3) engaging key hospital administrators and ICU leaders and frontline clinicians who will champion changes in PM&R practices and provide support for the program.^{46,50}

Equipment and Resources

Equipment and resources are required to introduce early PM&R in ICU patients. Standard equipment includes rolling intravenous poles with infusion pumps, walkers, and wheelchairs.^{46,55} A portable ventilator, cardiac monitor, and pulse oximeter can also facilitate ambulation of mechanically ventilated patients. When a portable ventilator is not available, other approaches include using a traditional (nonportable) ventilator on battery power or using a bag valve mask (BVM) with positive end-expiratory pressure valve and supplemental oxygen.

Personnel and Teamwork

Effective communication and coordination among ICU staff is important for early PM&R. In addition to rehabilitation clinicians, such as PT and OT, early PM&R requires teamwork from ICU physicians, nurses, and respiratory therapists. Additional PM&R members may include a speech language pathologist, physiatrist, and a technician or assistant for the PT and OT.^{56,57}

Adjuvant Interventions and Strategies

Several PM&R interventions are available, which may be useful for patients who are unable to participate in exercise programs due to physical limitations such as profound muscle weakness or are deeply sedated or in comatose, as described in this section.

Cycle ergometer. A cycle ergometer is a stationary bicycle that allows patients to receive passive, active-assisted, and active-resistive exercise. Bedside cycle ergometry has been

used safely in patients with severe COPD⁵⁸ and end-stage renal disease during dialysis.⁵⁹ In the ICU, cycle ergometry may be used with sedated, immobile, or awake patients to provide a range of motion (ROM) and strength muscle training.⁵⁵ In a randomized controlled trial of 90 mechanically ventilated patients with expected prolonged ICU stays, a 20-minute daily leg cycling session 5 days/week resulted in improved isometric quadriceps force, higher self-perceived functional status, and higher exercise capacity as measured by the 6-minute walk test at hospital discharge.⁶⁰

Fixed and dynamic tilt tables. A tilt table can allow partial weight bearing in a gravity-reduced environment for patients who require a graded transition from bed rest to supporting their full body weight. A dynamic tilt table allows movement of the table using a sled mechanism to permit flexion and extension of hips and knees against a partial body weight workload created by partial elimination of gravity when the device is tilted to <90° upright (eg, the table could be tilted as little as 10° above the horizontal plane). Although rigorous clinical research evaluations of such interventions in ICU patients have not yet been performed, they may help facilitate weight bearing, improve lower limb strength, and prevent ankle contractures.⁶¹⁻⁶⁴

Neuromuscular electrical stimulation. Neuromuscular electrical stimulation (NMES) has been used to reduce muscle atrophy and enhance muscle strength and endurance. This technique has been used as an alternative form of exercise in patients with severe chronic heart failure and chronic obstructive pulmonary failure.⁶⁵ In critically ill patients, NMES may elicit a systemic effect on peripheral microcirculation,⁶⁶ decrease muscle protein breakdown,⁶⁷ preserve muscle mass,^{68,69} and reduce ICUAW and weaning time.⁷⁰ Additional studies are needed to confirm these early findings.

Inspiratory muscle training. Inspiratory muscle training (IMT) may be beneficial in selected patients who fail ventilator weaning. There is some evidence that IMT improves maximum inspiratory pressure and reduces weaning time in selected ICU patients with prolonged mechanical ventilation.⁷¹ However, one study showed no benefit⁷² and IMT may not be generalizable to other ICU populations, such as those with chronic pulmonary obstructive pulmonary disease or congestive heart failure.⁷³ Further research is required to explore the patients who may most benefit from this intervention.

Early PM&R in the Neuro-ICU

The efficacy of inpatient rehabilitation is well established for neurological patients with stroke, spinal cord injury, multiple sclerosis, brain tumors, acquired brain injuries, and Guillain-Barré syndrome.⁷⁴⁻⁷⁷ However, early PM&R in the Neuro-ICU may not be routinely implemented due, in part, to the lack

of research investigating critical issues such as safety, feasibility, and overall benefits. The existing evidence supporting early PM&R has generally occurred within medical or medical-surgical ICUs. Given positive results in these ICUs, new investigation in the neuro-ICU is anticipated. In this section, we discuss some selected considerations in evaluating early PM&R in the Neuro-ICU setting.

Perceived Barriers

Neuro-ICUs may experience many of the same perceived barriers previously discussed. Important information is required regarding the safety of early PM&R in neurological patients as demonstrated in an anonymous survey of stroke clinicians evaluating their opinion on early mobilization after stroke. The survey demonstrated greater discomfort with mobilization of patients with hemorrhagic versus ischemic strokes, with 60% of respondents believing that there would be ill effects if mobilization occurred within 24 hours of stroke. Thus, establishing safety data in neuro-ICU patients is important for informing changes in practice.

Safety, Feasibility, and Benefit in Neuro-ICU

The effects of mobility on key neuro-ICU issues, such as intracranial pressure (ICP), cerebral blood flow (CBF), and cerebral perfusion pressure, have not been rigorously evaluated in prior studies. However, preliminary information supports early PM&R in certain populations. For instance, in a study of 20 participants with mild or moderate vasospasm after aneurysmal subarachnoid hemorrhage, gradual head of bed elevation of 20° and 45° did not result in significant changes in CBF when measured by transcranial Doppler.⁷⁸ Similarly, in a study of comatose and noncomatose neurosurgical participants with normal (<15 mm Hg) and elevated (> 15 mm Hg) ICP and stable neurologic status, passive and active ROM in a 30° head-up position had no effect or caused a modest decrease on ICP.⁷⁹ This preliminary information suggests that ROM and limb exercises can be performed safely in patients with normal or increased ICP provided there is no Valsalva-like maneuvers.⁷⁹

Researchers from Taiwan demonstrated that early and intensive rehabilitation of 154 participants with acute ischemic (60%) or hemorrhagic (40%) strokes in a neuro-ICU was feasible.⁸⁰ In this study, 44% and 45% of patients had moderate and severe strokes, respectively, and half of the patients started rehabilitation therapy within 4 days, receiving a mean of 0.6 (\pm 0.4) sessions/d.⁸⁰ This early and intensive rehabilitation resulted in improved functional outcomes with a mean improvement in the Barthel Index score of 33 points and 57% of patients walking independently at hospital discharge.⁸⁰ Data on early PM&R in other neuro-ICU populations are keenly awaited.

Finally, the A Very Early Rehabilitation Trial for Stroke (AVERT) demonstrated the feasibility and safety of very early

mobilization (VEM) for patients with acute stroke. In this trial, 71 patients with acute stroke admitted to specialized non-ICU acute stroke units were randomized to standard care (standard PT) versus standard care plus VEM (upright and out of bed twice daily within 24 hours of stroke for up to 14 days or until discharge).⁸¹ The median time to first mobilization after symptoms onset was significantly lower in the VEM group (18.1 vs 30.8 hours, $P < .001$), without any significant differences in the number of serious adverse events (15 vs 14, $P = .846$). Moreover, the VEM group returned to walking 50 m more quickly (median 3.5 vs 7.0 days, $P = .032$); and by 2 weeks, 67% of the VEM group (vs 50% of control group, $P = .032$) was able to walk unassisted.⁸²

Conclusions and Future Directions

Muscle weakness and impaired physical function are common and long lasting complications of critical illness. Currently, there are limited interventions to prevent these complications. However, in recent years, there is growing evidence that early PM&Rs are feasible, safe, and beneficial in critically ill patients. Such early interventions result in better functional outcomes at hospital discharge with further studies needed to evaluate the potential long-term benefits.

There is great potential for exploring the benefit of adjunctive interventions, such as use of cycle ergometry, dynamic tilt table, NMES, and IMT. Early and intensive mobilization of patients with acute stroke appears safe and leads to improved functional outcomes. However, greater investigation in neuro-ICU patients is required in future studies to understand whether the results of studies in other critically ill populations are applicable in the neuro-ICU patient populations.

Declaration of Conflicting Interests

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