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Early Mobilization and Rehabilitation of Patients Who Are Critically Ill

Mohamed D. Hashem, MD; Ann M. Parker, MD; and Dale M. Needham, FCPA, MD, PhD

Neuromuscular disorders are increasingly recognized as a cause of both short- and long-term physical morbidity in survivors of critical illness. This recognition has given rise to research aimed at better understanding the risk factors and mechanisms associated with neuromuscular dysfunction and physical impairment associated with critical illness, as well as possible interventions to prevent or treat these issues. Among potential risk factors, bed rest is an important modifiable risk factor. Early mobilization and rehabilitation of patients who are critically ill may help prevent or mitigate the sequelae of bed rest and improve patient outcomes. Research studies and quality improvement projects have demonstrated that early mobilization and rehabilitation are safe and feasible in patients who are critically ill, with potential benefits including improved physical functioning and decreased duration of mechanical ventilation, intensive care, and hospital stay. Despite these findings, early mobilization and rehabilitation are still uncommon in routine clinical practice, with many perceived barriers. This review summarizes potential risk factors for neuromuscular dysfunction and physical impairment associated with critical illness, highlights the potential role of early mobilization and rehabilitation in improving patient outcomes, and discusses some of the commonly perceived barriers to early mobilization and strategies for overcoming them.

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Early mobilization and rehabilitation of patients who are critically ill have received growing attention because of increasingly recognized sequelae of neuromuscular dysfunction and physical impairment associated with critical illness. This topic will be discussed in the following sections: (1) acquired neuromuscular disorders in the ICU, (2) risk factors for neuromuscular disorders and functional impairment, (3) sequelae of neuromuscular disorders, (4) safety of early mobilization and rehabilitation, (5) benefits of early mobilization and rehabilitation, (6) commonly perceived barriers to early mobilization and rehabilitation, and (7) future directions.

ABBREVIATIONS: CIM = critical illness myopathy; CIP = critical illness polyneuropathy; CRRT = continuous renal replacement therapy; ETT = endotracheal tube; ICUAW = ICU-acquired weakness; IQR = interquartile range; LOS = length of stay; MICU = medical ICU; MMT = manual muscle testing; NMB = neuromuscular blocker; NMES = neuromuscular electrical stimulation; OT = occupational therapy; PT = physical therapy; QI = quality improvement; RCT = randomized controlled trial

AFFILIATIONS: From the Outcomes After Critical Illness and Surgery (OACIS) Group (Drs Hashem, Parker, and Needham); and the Division of Pulmonary and Critical Care Medicine (Drs Hashem, Parker, and Needham) and the Department of Physical Medicine and Rehabilitation (Dr Needham), School of Medicine, Johns Hopkins University, Baltimore, MD.

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CORRESPONDENCE TO: Dale M. Needham, FCPA, MD, PhD, Pulmonary and Critical Care Medicine, Johns Hopkins University, 1830 E Monument St, 5th Floor, Baltimore, MD 21205; e-mail: dale.needham@jhmi.edu

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Acquired Neuromuscular Disorders in the ICU

One of the earliest published reports on neuromuscular dysfunction in the ICU was a case series of five patients with flaccid limbs, loss of reflexes, and delayed weaning from mechanical ventilation.[1] Electrophysiological testing revealed a primary axonal polyneuropathy, with sparing of the central nervous system. These findings led to the term *critical illness polyneuropathy* (CIP).[2] CIP is characterized by reduced sensory nerve action potentials and compound muscle action potentials, with normal or mildly reduced nerve conduction velocity.[3,4] The complex underlying pathophysiology may include dysfunction of microvascular circulation of the endoneurium with increased permeability and extravasation of activated leukocytes.[5]

Critical illness myopathy (CIM) is another manifestation of neuromuscular dysfunction that includes thick filament (myosin) loss,[6] as well as myofiber necrosis and atrophy.[4,7,8] This loss of muscle mass may result from increased muscle proteolysis mediated by enhanced ubiquitin-proteasome system activation, combined with decreased muscle protein synthesis.[4] Importantly, despite their distinct definitions, CIP and CIM often coexist.[9]

ICU-acquired weakness (ICUAW) refers to clinically detectable muscle weakness in patients who are critically ill, in the absence of weakness caused by factors other than critical illness.[8] Approximately one-third of patients who are critically ill have ICUAW.[10] Possible etiologies may include muscle atrophy or wasting, CIP, CIM, or a combination of these factors.[11] ICUAW is diagnosed by means of manual muscle testing (MMT), whereby six different muscle groups are assessed bilaterally by using the six-point ordinal Medical Research Council scale,[12] with a sum score ranging from 0 (no visible or palpable contraction in all 12 muscle groups) to 60 (normal strength), with ICUAW typically defined as a sum score < 48.[3,8] Although MMT is feasible and easily administered, it requires the patient to be awake, cooperative, and able to follow commands.[13] In addition, being an ordinal scale, this measure is limited in its ability to detect clinically meaningful differences in strength.[11]

Other tests that might play a role in diagnosing muscle weakness include handgrip dynamometry and handheld dynamometry. In a prospective cohort study of 136 patients receiving mechanical ventilation, handgrip strength showed good correlation with MMT and an independent association with in-hospital mortality.[14] Handheld dynamometry is a small force measurement device that fits into the palm of the hand of the examiner and is used as part of a standardized physical examination to measure volitional strength on a continuous scale.[15,16] However, it generally requires the tested muscle to move against gravity (minimum score of 3 on MMT) and can be fatiguing when performed in patients who are weak, which can potentially limit feasibility in patients who are critically ill.[15]

Risk Factors for Neuromuscular Disorders and Functional Impairment

We will briefly summarize available evidence on the following commonly cited risk factors for neuromuscular disorders and functional impairment: bed rest, corticosteroids, and neuromuscular blockers (NMBs).

Bed Rest

Young healthy adults subjected to bed rest can have substantial loss of muscle mass and strength within a short time.[17,18] In patients who are critically ill, bed rest also has a strong association with muscle weakness. A prospective study longitudinally followed 222 survivors of ARDS for 2 years.[19] After adjusting for 18 variables, including baseline characteristics and potential risk factors for muscle weakness, the duration of bed rest in the ICU was the only risk factor with a strong, independent, and consistent association with muscle weakness across the entire follow-up. Over 3-, 6-, 12- and 24-month follow-up assessments, there was a 3% to 11% relative decrease in muscle strength for each additional day of bed rest in the ICU.[19] Another prospective study longitudinally followed 203 survivors of ARDS from 12 hospitals in the ARDS Network for 12 months after discharge.[20] After adjusting for age, sex, comorbidities, and baseline functional status, ICU length of stay (LOS) had a significant and independent association with decreased muscle strength. Importantly, ICU LOS approximated the duration of bed rest because 75% of patients did not routinely receive early mobilization in their ICUs.[20]

Bed rest is very common in routine clinical practice in the ICU setting. Across point prevalence studies from the United States, Germany, Australia, and New Zealand, the vast majority of patients receiving mechanical ventilation did not receive any form of out-of-bed mobilization.[21-23]

Corticosteroids

There are mixed results in studies evaluating systemic corticosteroids and physical sequelae in patients who are critically ill. For instance, in a study of 95 patients receiving mechanical ventilation, administration of corticosteroids before awakening was a strong independent predictor of ICUAW at awakening (OR, 14.9; 95% CI, 3.2-69.8; $P < .001$); however, there was no association with dose or duration of corticosteroids.[3] A prospective study following 203 survivors of ARDS for 1 year reported a significant association between higher mean corticosteroid dosage (up to 40 mg/d of prednisone equivalent) in the ICU and decreased percentage in predicted 6-minute walk distance ($P = .032$) and ShortForm-36 Health Survey[24] physical function domain ($P = .005$) scores, but not muscle strength (measured via MMT), in a multivariable regression model that adjusted for baseline characteristics, comorbidities, and premorbid functional status.[20] In contrast, the previously mentioned 2-year follow-up study of 222 survivors of ARDS found no association between cumulative dose of corticosteroids in the ICU and weakness or any other physical outcome measure.[19]

Neuromuscular Blockers

Mixed results also have been reported in studies evaluating NMBs. For instance, in a subanalysis of 1,200 patients who were critically ill who were enrolled in a randomized controlled trial (RCT) evaluating intensive insulin therapy, infusion of NMBs was an independent risk factor for the presence of abundant spontaneous activity at electromyography (OR, 2.01; 95% CI, 1.1-3.99; $P = .02$).[25] However, a multicenter RCT randomly assigned 340 patients with severe ARDS to receive either cisatracurium infusion for 48 hours or placebo, starting within 48 hours of ARDS onset. No significant difference was found between the two groups in the median Medical Research Council score or the prevalence of ICUAW at ICU discharge or day 28.[26] Moreover, there was no association of NMB use (ever vs never) with muscle weakness in two observational longitudinal follow-up studies of survivors of ARDS described earlier.[19,20] However, only a minority of patients in these observational studies received NMBs.

Sequelae of Neuromuscular Disorders

ICU-associated neuromuscular disorders have short- and long-term sequelae. Several studies reported an association between ICUAW and delayed weaning from mechanical ventilation, increased in-hospital costs, and increased mortality.[14,27-29] In addition, patients with ICUAW may have a significantly increased risk of death after discharge[29-31] and significant impairments in respiratory muscle strength, physical function, and health-related quality of life that persist for at least 2 years.[19] Persistent physical impairment was also reported in other longitudinal studies that followed survivors of ARDS up to 5 years after discharge.[32,33] As discussed in the subsequent sections, increasing recognition of these sequelae and their long-lasting effects has intensified interest in early mobilization and rehabilitation as a potential intervention to improve patient outcomes.

Safety of Early Mobilization and Rehabilitation

Patients receiving mechanical ventilation are often considered to have a vulnerable hemodynamic and respiratory status, among other perceived barriers, that may interfere with mobilization. However, the reported rate of adverse events is very low, mostly in the form of transient physiological derangements that resolve without the need for any additional therapy.[34-36] There is expert consensus that early mobilization and rehabilitation are safe and do not expose patients receiving mechanical ventilation to any significant additional risk, as long as they are closely monitored during and after mobilization.[37-39]

Benefits of Early Mobilization and Rehabilitation

There is variability in the results of clinical trials evaluating early mobilization and rehabilitation, with some studies demonstrating substantial benefits and others showing no significant benefit (Table 1).[40-45] For instance, a quasi-RCT showed that early mobilization, initiated within 48 hours of intubation, resulted in a significantly reduced number of days to first mobilization out of bed and reduced ICU and hospital LOS.[40] Similarly, in a two-center RCT, starting physical therapy (PT) and occupational therapy (OT) early (at a median of 1.5 days after intubation) resulted in a shorter duration of delirium and mechanical ventilation, as well as a significant increase in functional independence at hospital discharge.[41] In addition, as discussed later, trials evaluating the use of rehabilitation devices, such as cycle ergometry and neuromuscular electrical stimulation (NMES), in the ICU setting have demonstrated some evidence of benefit (Table 1).[40-45]

However, in a single-center RCT in patients in the ICU for ≥ 5 days, intensive exercise in the ICU

TABLE 1] Summary of Selected Controlled Clinical Trials of Rehabilitation Interventions in the ICU

Study/Year	Type	No. of patients	Intervention	Control	Key Outcomes	Results (Intervention vs Control)
Trials With Positive Outcomes						
Morris et al[40]/ 2008	Quasi-randomized controlled trial single-center MICU	330	A mobility protocol carried out by a dedicated mobility team (ICU nurse, nursing assistant, physical therapist)	PT directed by the primary team	a. Proportion of patients receiving PT intervention in ICU b. Days to first out of bed, mean c. ICU LOS, mean d. Hospital LOS, mean e. Ventilator days, mean	a. 91% vs 13%; $P \leq .001$ b. 5 vs 11 d; $P < .001$ c. 6 vs 7 d; $P = .025$ d. 11 vs 15 d; $P = .006$ e. 9 vs 10 d; $P = .163$
Schweickert et al[41]/ 2009	RCT, MICUs in 2 hospitals	104	Early PT and OT intervention starting within 72 h of MV	PT and OT directed by the primary team	a. Time from intubation to PT and OT, median b. Return to independent function at discharge c. Proportion of time in ICU with delirium d. Ventilator-free days, median e. Proportion of patients discharged home	a. 1.5 vs 7.4 d; $P < .0001$ b. 59% vs 35%; $P = .02$ c. 33% vs 57%; $P = .02$ d. 24 vs 21; $P = .05$ e. 43% vs 24%; $P = .06$
Burtin et al[42]/ 2009	RCT, medical and surgical ICUs at 1 hospital	90	In-bed cycle ergometry starting at average 14 d from admission	Standard mobilization 5 d/wk	a. 6MWD at hospital discharge, median b. SF-36 physical function score at discharge, median c. Quadriceps force at hospital discharge, mean	a. 196 vs 143 m; $P < .05$ b. 21 vs 15 points; $P < .01$ c. 2.4 vs 2 $N \cdot kg^{-1}$; $P < .05$
Routsi et al[43]/ 2010	RCT, single-center mixed ICU	140	Daily NMES	No NMES	a. Proportion of patients with ICUAW b. ICU LOS, mean c. Ventilator-free days, median	a. 13% vs 39%; $P = .04$ b. 14 vs 22 d; $P = .11$ c. 4 vs 6 d; $P = .003$
Trials With Negative Outcomes						
Denehy et al[44]/ 2013	RCT, single-center mixed ICU	150	Physiology-based mobilization 15 min/d while receiving MV, then 2 × 15 min/d after weaning	PT available 12 h/d, 7 d/wk	a. 6MWD 12 mo after ICU discharge, mean b. SF-36 physical function score at 12 mo, mean c. Difference in rate of change in 6MWD,[a] mean	a. 434 vs 410 m; NS b. 41 vs 44 points; NS c. 2.95 m/wk; $P = .049$[a]
Moss et al[45]/ 2015	RCT, MICUs and SICUs in 5 hospitals	120	Intensive PT intervention 7 d/wk in ICU and ward, with mean duration of 31 min	ROM, positioning, mobility 3 d/wk in ICU and ward, with mean duration of 21 min	a. PFP-10 score at 1 mo, mean b. SF-36 physical function score at 1 mo, median c. Timed Up and Go test at 1 mo, mean d. ICU LOS, median e. 28-day hospital-free days, median	a. 20 vs 21; $P = .73$ b. 35 vs 50 points; $P = .15$ c. 15.6 vs 15.2 s; $P = .9$ d. 15 vs 16 d; $P = .69$ e. 7 vs 7 d; $P = .97$

ICUAW = ICU-acquired weakness; LOS = length of stay; MICU = medical ICU; MV = mechanical ventilation; NMES = neuromuscular electrical stimulation; NS = not significant; OT = occupational therapy; PFP-10 = Physical Functional Performance 10-item test; PT = physical therapy; RCT = randomized controlled trial; ROM = range of motion; SF-36 = ShortForm-36 Health Survey; SICU = surgical ICU; 6MWD = 6-minute walk distance.

[a]Difference in rate of change in 6MWD between intervention and control groups over 12 months of follow-up.

(started at a median [interquartile range (IQR)] of 7 [5-11] days from admission),[46] along with more intensive exercise on the hospital ward and in the outpatient setting, did not improve patient outcomes compared with usual care over a 1-year follow-up.[44] Moreover, a five-center RCT, starting an intensive PT program at a median (IQR) of 8 (6-11) days after intubation, also did not improve physical functioning during 1-, 3-, and 6-month follow-up.[45] In contrast to the trials in the prior paragraph showing positive outcomes, in both of these trials initiation of the rehabilitation intervention was relatively delayed, with both starting the intervention at the same time as the control group in a prior positive trial.[41] In addition, the intensity of PT intervention in the control group in both trials was greater than in the control groups of the positive controlled trials and the usual care practices in many ICUs on the basis of point prevalence studies (Table 2).[21-23,30,40,41,44,45] Standardized reporting of usual care in future clinical trials will play an important role in improving comparisons between studies.[47]

Multiple quality improvement (QI) projects worldwide have successfully implemented early mobilization and rehabilitation in ICU settings (Table 3).[48-53] Overall, these projects have demonstrated the safety and feasibility of early mobilization and rehabilitation, as well as multiple potential benefits, such as decreasing ICU and hospital LOS.[54]

TABLE 2] Mobilization of Patients Receiving Mechanical Ventilation Among Selected Observational Studies and Control Groups of Clinical Trials

Study/Country/Year	Study Type and No. of Sites	Patients	Mobility Status Achieved and Rehabilitation Delivered
Observational Studies of Usual Practice			
Berney et al[21]/ Australia/New Zealand/2013	1-d point prevalence study in 38 ICUs in 38 hospitals	N = 200 in ICU for > 2 d	• 0% of patients stood, sat out of bed, or walked
Nydahl et al,[22]/ Germany/ 2014	1-d point prevalence study in 116 ICUs in 115 hospitals	N = 401 with ETT	• 2% of patients sat in chair or marched in place, with no walking
Jolley et al[23]/ United States/ 2015	2-d point prevalence study in 33 ICUs in 17 hospitals	N = 566 (77% with ETT)	• 10% of patients stood, marched in place, or walked
Hodgson et al[30]/ Australia/New Zealand/2015	Prospective cohort (with up to 14 d of evaluation) in 12 ICUs in 12 hospitals	N = 192 with expected MV > 2 d	• 36% of patients received any PT involving active participation, with 18% starting at ≤ 5 d • 3% of PT included standing, sitting out of bed, marching, or walking • Mean 1.1 PT session per patient while receiving mechanical ventilation in ICU
Control Groups From Clinical Trials With Positive Results			
Morris et al[40]/ United States/ 2008	Quasi-RCT: usual care in 7 ICUs in 1 hospital	N = 135 in MICU, enrolled within 2 d of MV	• 6% of patients received PT in ICU
Schweickert et al[41]/United States/2009	RCT: usual care in 2 MICUs in 2 hospitals	N = 55 with ETT, enrolled within 3 d of MV	• Median (IQR) duration of PT and OT during MV of 0 (0-0) min/d • PT initiated at median (IQR) of 7 (6-11) d after intubation
Control Groups From Clinical Trials With Negative Results			
Denehy et al[44]/ Australia/2013	RCT: usual care in single ICU	N = 76 in ICU for > 5 d (~92% MV)	• PT available 12 h/d, 7 d/wk • 52% mobilized out of bed while in ICU[a]
Moss et al[45]/ United States/ 2015	RCT: protocolized PT in 5 hospitals	N = 61 enrolled after MV for ≥ 4-5 d	• PT per protocol: 20 min, 3 × wk in ICU • Actual PT: mean ± SD 3.8 ± 2.4 PT sessions of 21 ± 3.2 min per patient in ICU • 74% of patients received sitting and/or standing exercises in ICU and ward • 80% of patients received functional mobility training in ICU and ward

ETT = endotracheal tube; IQR = interquartile range. See Table 1 legend for expansion of other abbreviations.
[a]As reported in the trial, these data are based on a point prevalence evaluation that included 68 patients receiving MV at the study site who were not enrolled in the trial and received usual care.

TABLE 3] Summary of Selected QI Projects of Early Mobilization and Rehabilitation Interventions in the ICU

QI Project Location/ Year	ICU	Patient Population and Time Frame	Selected Aspects of the QI Intervention	Key Outcomes (Before vs After QI)
Johns Hopkins Hospital[48]/ 2010	16-bed MICU	N = 576, QI executed over 4 mo	• Adopting the 4Es model[a] of QI[49,50] • Changing default activity level from bed rest to as tolerated • Discouraging sedation infusions for as needed boluses • Establishing simple PT and OT and safety guidelines	• No. of PT and OT treatments in ICU, mean (1.6 vs 4.3; $P < .05$) • ICU LOS, mean (7 vs 5 d; $P = .02$) • PT and OT treatment of sitting or greater (56% vs 78%; $P = .03$, based on a subset of 344 treatments)
University of California San Francisco[51]/ 2013	16-bed mixed ICU	N = 373, QI executed over 9 mo	• Establishing an early mobilization working group, with monthly meeting • Distributing standards for PT interventions and exclusion guidelines to all ICU staff • Changing patient selection for PT to become an interprofessional process instead of being physician driven • Assessing mobility daily in coordination with nurses, physical and respiratory therapists	• Patients ambulating (43% vs 50%; $P = .004$) • Patients discharged home (55% vs 77%; $P < .001$) • ICU LOS, median (6 vs 4 d; $P = .011$)
University of Alabama at Birmingham[52]/ 2013	28-bed trauma and burns ICU	N = 2,176, QI executed over 12 mo	• PT referral on ICU admission • 4-level mobility program ranging from positioning and PROM to walking • Daily rounds, mobility flow sheets	• PT billable units per day, mean (11 vs 21) • ICU LOS, mean (11 vs 10 d; $P = .33$) • Prevalence of deep vein thrombosis (11% vs 7%; $P \leq .001$) • Prevalence of pneumonia (28% vs 22%; $P \leq .01$)
University Hospitals Birmingham, England[53]/ 2015	75-bed mixed ICU	N = 582, MV ≥ 5 d, QI executed over 12 months	• Adopting the 4Es model of QI[49,50] • Creating a critical care physiotherapy subteam • Transcribing rehabilitation plans onto wall charts • Conducting weekly rehabilitation meetings	• Time to first mobilization, mean (9 vs 6 d; $P = .001$) • ICU LOS, mean (17 vs 14 d; $P = .007$)

PROM = passive range of motion; QI = quality improvement; RN = registered nurse; See Table 1 legend for expansion of other abbreviations.
[a]The 4Es model is part of a structured quality improvement model that consists of engaging and educating stakeholders followed by executing the intervention and then evaluating results in an iterative manner

Commonly Perceived Barriers to Early Mobilization and Rehabilitation

We will discuss some commonly perceived barriers to early mobilization and rehabilitation, as well as potential strategies to overcome them.[55]

Cultural Barriers

In many centers, current ICU culture is an important and potentially modifiable barrier to early mobilization and rehabilitation. Insufficient coordination, timing conflicts with different procedures, and competing patient priorities are common.[21,46,56,57] Overcoming these barriers requires a structured multidisciplinary effort, with clear communication and recognition of the importance of early mobilization and rehabilitation.[58] Provision of critical care in an ICU with a culture that prioritizes early rehabilitation increases the number of patients receiving mechanical ventilation ambulating by threefold.[59,60]

A structured QI model in the Johns Hopkins Hospital medical ICU (MICU) was used to change the culture and implement early rehabilitation for all patients.[48] Key components of this project included creating PT and OT consultation guidelines, as well as changing patient activity and sedation practices (Table 3).[48-53] Ongoing implementation and evaluation of the project was performed through weekly meetings with all members of the multidisciplinary team.[48,49] Through this process, there was a large decrease in the proportion of ICU days in which eligible patients did not receive PT and OT interventions (41% vs 7%; $P = .004$),[48] with improvement in the timing of early PT interventions sustained for at least 5 years after completion of the QI project.[61] Qualitative research conducted with the staff in the MICU revealed that this QI project led to early mobilization and rehabilitation being perceived as common sense and was associated with increased staff satisfaction.[62]

Sedation

The widespread use of sedation in the ICU can be a major barrier to mobilizing patients who are critically ill.[23,30,63,64] Sedation minimization can be combined with early mobility via implementing the ABCDE bundle,[65] in which all patients undergo daily coordinated spontaneous awakening trials, spontaneous breathing trials, sedation and delirium screening, and early mobility and rehabilitation.[66-68] A pre-post prospective study in 296 patients showed that applying this bundle was feasible and improved patient outcomes, such as reducing delirium and increasing mobilization out of bed.[66]

Endotracheal Tubes

The presence of an endotracheal tube (ETT) is another commonly perceived barrier.[30] To assist with overcoming this barrier, one study detailed the steps undertaken to start PT and OT interventions after a median of only 1.5 days of intubation in 49 patients who had undergone endotracheal intubatation.[69] Patients underwent daily screening for 10 contraindications to PT and OT interventions, followed by daily interruption of sedation until they achieved wakefulness, with PT and OT interventions initiated thereafter. Initiation of PT and OT interventions was preceded by securing the ETT, removing unnecessary noninvasive devices, and disconnecting enteral feedings tubes. Rehabilitation interventions were completed on 90% of patient days. One-third of sessions involved patients who had undergone intubation moving from bed to chair and standing, and 15% involved patients who had undergone intubation ambulating. Therapy was stopped prematurely in only 4% of all sessions, mostly because of ventilator dyssynchrony.[69] Figure 1 illustrates a patient receiving mechanical ventilation via an ETT and ambulating with a physical therapist in the ICU.

Femoral Catheters

Femoral catheters are a perceived barrier to early rehabilitation because of the risk of accidental removal, bleeding, or infection.[30] However, investigators in one study observed 101 patients in the MICU with a femoral catheter (81% venous, 29% arterial, and 6% hemodialysis) who had 253 PT sessions over 210 ICU days. Patients were able to perform in-bed

Figure 1 – *Photo showing a patient receiving mechanical ventilation via an endotracheal tube while ambulating in the ICU with a physical therapist. (The patient provided written consent for the use of this photograph.)*

exercises, supine cycle ergometry, and stand or walk on 38%, 12%, and 23% of days, respectively. There were no catheter-related adverse events.[70] Similar results were obtained in other studies.[71,72]

Continuous Renal Replacement Therapy

The use of continuous renal replacement therapy (CRRT) is another perceived barrier.[21] However, a prospective single center study including 57 consecutive patients (79% receiving mechanical ventilation) who received at least one PT session while undergoing CRRT demonstrated no safety events associated with CRRT.[73] A total of 268 PT sessions included in-bed exercises (29%), supine cycle ergometry (27%), sitting on the edge of the bed (30%), transferring to a chair (5%), and standing or marching in place (9%). Similar results were obtained in another prospective study that also demonstrated potential improved CRRT filter life with patient mobilization.[74]

Costs

Increased staffing and costs associated with early rehabilitation are commonly perceived barriers. A controlled trial using a dedicated mobility team did not result in increased overall costs after accounting for extra costs related to the mobility team,[40] with evidence of significantly decreased risk of readmission or death in the year after ICU dishcarge.[75] Similarly, a QI project demonstrated a significant decrease in average MICU and hospital LOS.[48] Using data from the QI project and other publications, a financial model for introducing ICU early mobilization and rehabilitation had 24 possible scenarios (ranging from conservative to best-case scenarios), 83% of which had net savings.[76]

Future Directions

Novel use of existing equipment and devices may assist with early rehabilitation in the ICU setting. For instance, NMES uses skin electrodes to deliver electrical stimuli to arm and leg muscles,[77] with the goal of producing visible contraction.[78] Studies using NMES in patients in the ICU have consistently reported that it is safe and feasible and may have potential benefit in improving muscle mass, strength, and function.[78-81] On the basis of evaluation in healthy subjects, the beneficial effects of NMES may be mediated, in part, through changes in cytokines, similar to changes observed after active exercise.[82]

In-bed cycle ergometry also has been successfully used with patients who are critically ill. An RCT assigned 90 patients who were critically ill to receive either usual care or bedside cycling starting at ≥ 5 days after admission.[42] Patients in the intervention group had significantly better outcomes at hospital discharge (Table 1).[40-45] Exercise was terminated early in < 4% of sessions because of transient physiological derangements that resolved within 2 minutes of exercise cessation.[42] A prospective cohort study in 181 patients (82% receiving mechanical ventilation) receiving 541 cycle ergometry sessions reported a 0.2% rate of potential safety events or physiological changes.[83]

Combining NMES with bedside cycling may have the advantage of engaging patients in active cycling at an early stage of critical illness. This technique, called *functional electrical stimulation cycling*, was evaluated in a small pilot study of eight patients receiving mechanical ventilation,[84] with a larger multicenter RCT currently being conducted to assess the efficacy of functional electrical stimulation cycling in improving short- and long-term physical and cognitive outcomes (ClinicalTrials.gov identifier NCT02214823). Single center reports also have highlighted interactive video games and hydrotherapy (ie, rehabilitation in a swimming pool) as innovative ideas for ICU rehabilitation.[85,86]

Conclusions

ICU-associated neuromuscular disorders are increasingly being recognized as contributing to short- and long-term physical impairments. Bed rest has a strong association with neuromuscular dysfunction and physical impairments, and early mobilization and rehabilitation may be valuable interventions to mitigate these sequelae. Despite the many perceived barriers, mobilization and rehabilitation, when started shortly after mechanical ventilation, are safe, feasible, and potentially beneficial in improving patients' functional outcomes and decreasing mechanical ventilation duration and LOS.

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