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Mobilizing Patients in the Intensive Care Unit

Improving Neuromuscular Weakness and Physical Function

Dale M. Needham, MD, PhD

Early mobilization of patients in the hospital and the intensive care unit has a strong historical precedent. However, in more recent times, deep sedation and bed rest have been part of routine medical care for many mechanically ventilated patients. A growing body of literature demonstrates that survivors of severe critical illness commonly have significant and prolonged neuromuscular complications that impair their physical function and quality of life after hospital discharge. Bed rest, and its associated mechanisms, may play an important role in the pathogenesis of neuromuscular weakness in critically ill patients. A new approach for managing mechanically ventilated patients includes reducing deep sedation and increasing rehabilitation therapy and mobilization soon after admission to the intensive care unit. Emerging research in this field provides preliminary evidence supporting the safety, feasibility, and potential benefits of early mobilization in critical care medicine.

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CASE PRESENTATION

DR NEEDHAM: Mr E is a 56-year-old man with severe chronic obstructive pulmonary disease. He was recently admitted to the Johns Hopkins Hospital (Baltimore, Maryland) with acute renal failure. Three days later, he was transferred to the medical intensive care unit with acute respiratory failure requiring mechanical ventilation. Mr E had a complicated 2-month medical intensive care unit stay that included aspiration, sepsis, and significant weight loss. He was discharged from the medical intensive care unit to an acute rehabilitation facility for ventilator weaning and physical rehabilitation. After approximately 6 weeks in rehabilitation, he was discharged home.

MR E: Thank you for coming today. Can you tell us about your quality of life before hospital admission?

MR E: Well, I enjoyed life thoroughly. I went out to dinner with friends, went grocery shopping, and had a wonderful time.

DR NEEDHAM: In the intensive care unit, patients frequently receive bed rest. What is that like?

MR E: It was unbearable—always being on my back and having the nurses do everything for me. You lose your dignity. I wanted to get out of bed and do something; otherwise, I was laying there saying "Why me?"

DR NEEDHAM: What did you think when we discussed getting you out of bed while on a ventilator with a breathing tube in your mouth?

MR E: I thought it was wonderful. Anything to get me up and moving, and get me out of bed; anything to get me off my back and on my feet—that is what I really wanted.

DR NEEDHAM: How did it feel to be awake, with the breathing tube in your mouth, on a ventilator, and walking laps around the medical intensive care unit?

MR E: It was wonderful. It was nice to get up and walk around. It was not uncomfortable. I enjoyed it. I think it had a very positive effect on me.

DR NEEDHAM: What is your quality of life like since being discharged home?

MR E: Wonderful. I am able to walk around my apartment, make my own food, and bathe myself. I can get outdoors when I want to.

CME available online at www.jamaarchivescme.com and questions on p 1709.

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Historical Background of Early Mobilization

The early ambulation of hospitalized patients was first introduced late during World War II in an effort to expedite the recovery of soldiers for return to the battlefield.[1] The first conferences on bed rest were published in 1944.[2] Leading international journals also published related editorials with explicit titles, such as "The Evil Sequelae of Complete Bed Rest."[3] According to such publications, the benefits of early ambulation were clear: "First, morale is greatly improved. . . . General health and strength are better maintained and convalescence is more rapid."[4]

Years later, intensive care units (ICUs) were created. Intensive care physician Thomas Petty, MD, provides a vivid comparison of medical care in ICUs at present vs at the inception of critical care[5]:

When I make rounds in critical care units . . . what I see these days are paralyzed, sedated patients, lying without motion, appearing to be dead, except for the monitors that tell me otherwise . . . This was not the case in past. . . .

When we first started our unit in 1964, patients who required mechanical ventilation were awake and alert and often sitting in a chair . . . these individuals could interact . . . they could feel human. . . . By contrast, patients with induced coma . . . cannot even maintain muscular tone . . . and muscle atrophy begins.

The requirement of high acuity care and available pharmacologic therapy has led to the present situation . . . the awake and alert patient who is anxious or depressed requires a great amount of interaction with the health care team. . . . Understanding of the delicate machine/patient interface seems to be lost these days; thus, the requirement of sedation and paralysis.

In 1972, the University of Colorado published a photo-illustrated report describing ambulation of a mechanically ventilated patient recovering from respiratory failure. In this report, the perceived benefit of early mobilization of ICU patients was clear:

The therapeutic value of this early ambulation has been well documented in our ICU by the improved sense of well-being and the increased general strength the patient develops from physical activity.[6]

Another publication in 1975 from Geisinger Medical Center, in Danville, Pennsylvania, provides similar historical evidence of early ambulation for ICU patients:

. . . early ambulation is clinically useful . . . . Patient acceptance has been excellent. It is our impression that by early ambulation, weaning has been facilitated and hastened, and the problems of prolonged bed and chair rest minimized.[7]

Thus, despite the current culture of deep sedation and bed rest in many ICUs, there is a historical basis for early mobilization of both hospitalized and critically ill patients.

Epidemiology of Neuromuscular Dysfunction

The interest in early mobilization within critical care medicine arises from recent publications that vividly describe the neurological complications faced by ICU survivors, particularly those with severe critical illness and prolonged mechanical ventilation. The problems facing some intensivists and their patients is well described by Charles Bolton, MD, and G. Bryan Young, MD[8]:

As intensivists struggle to overcome the complex problems of sepsis and multiple organ failure, these nervous system complications are either overlooked or misdiagnosed. [Consequently,] the patient is discharged to a general ward, where the patient experiences impaired cognition; difficult dressing, eating and rising from the bed or toilet seat; difficulty standing and walking; shortness of breath; and fatigue. A prolonged stay in a rehabilitation center may be necessary.

To understand the prevalence and effects of neuromuscular dysfunction in critical illness, my colleagues and I[9] performed a systematic review of reports on adult ICU patients who were evaluated both clinically and electrophysiologically. In 24 eligible studies, which focused on ICU patients with sepsis, multiorgan failure, or prolonged mechanical ventilation, neuromuscular dysfunction was identified in 655 of 1421 patients (46%) and was associated with prolonged duration of mechanical ventilation and length of ICU and hospital stay. One of the largest studies in this field, which defined weakness based on clinical examination rather than electrophysiological criteria, reported an incidence of neuromuscular weakness of 25% in patients who were mechanically ventilated for 7 days or longer and awakened to allow examination. The mean duration of mechanical ventilation after awakening was longer in patients with vs without weakness (18 vs 8 days; $P = .03$).

In a landmark study of patient long-term outcomes after acute respiratory distress syndrome (ARDS), Herridge et al[10] observed that patients lost, on average, 18% of their body weight in the ICU. The median 6-minute walk distance in survivors was only 66% of predicted at 1 year after ICU discharge, with limitations attributed to ICU-acquired morbidities, such as global muscle wasting and weakness, foot drop, joint immobility, and dyspnea. Only 49% of survivors had returned to work at 1 year. Thus, in severe critical illness, neuromuscular dysfunction, muscle weakness, and impaired physical function are common and severe.

To understand quality of life (QOL) outcomes in ICU and ARDS survivors, my colleagues and I performed a systematic review[11] and a meta-analysis.[12] The meta-analysis[12] included 5 published studies[10,13-16] that used the Medical Outcomes Study Short-Form 36 QOL instrument at 1 to 4 years after ARDS.[12] This meta-analysis demonstrated similar QOL findings across the 5 studies despite variability in ARDS risk factor, study location, and follow-up time interval. In particular, when compared with age- and sex-matched population norms, decrements in the QOL of ARDS survivors related to the physical function and physical role domains were large and persistent. The reason for these QOL decrements is likely multifactorial and includes impaired pulmonary function,[15,17] loss of muscle bulk, proximal weakness, and fatigue.[10]

Etiology and Pathogenesis of Neuromuscular Weakness

The etiology and pathogenesis of ICU-acquired neuromuscular weakness are

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multifactorial.[18,19] Critical illness polyneuropathy and/or myopathy is a well-recognized etiology.[9,20] Inflammation associated with common ICU conditions, such as sepsis, also may be associated with muscle dysfunction, especially in the setting of immobility.[21] Bed rest, alone, is another important etiology with experimental studies demonstrating that healthy, well-nourished individuals experience a 4% to 5% loss of muscle strength for each week of bed rest.[22] Of these causes of weakness, early mobilization of ICU patients may most directly modify the negative effects of bed rest, which are discussed in more detail in the next section.

Detrimental Effects of Bed Rest

Bed rest results in changes in muscle fibers, inflammatory markers, and metabolic parameters. During bed rest, disuse atrophy occurs in skeletal muscle. Moreover, myosin isoforms change from slow to fast twitch fibers, metabolism changes from fatty acids to glucose, and protein synthesis is decreased.[23-25] Muscle activity also may play an anti-inflammatory role, which may be beneficial in inflammation-mediated diseases of critical illness, such as ARDS and sepsis.[26] In addition, experimental research has demonstrated that after only 5 days of bed rest, healthy individuals developed insulin resistance and microvascular dysfunction, which may be especially detrimental to ICU patients.[27]

The physiological harms of bed rest are not limited to the musculoskeletal system. There is a wealth of literature, primarily from aerospace research, demonstrating the effects of bed rest on nearly every body system.[28] The effects that are potentially relevant to ICU patients include fluid losses, contributing to postural hypotension and tachycardia, and decreased stroke volume, cardiac output, and peak oxygen uptake, all of which have been observed in healthy volunteers undergoing bed rest.[28-30] Even in these healthy volunteers, there is a prolonged recovery period required after cessation of bed rest before return to baseline status.[28,29]

Clinical Presentation and Evaluation

Given the high prevalence of deep sedation and bed rest for mechanically ventilated patients in the ICU,[31] neuromuscular weakness is often recognized late when there is difficulty liberating a patient from mechanical ventilation, or once a patient has been discharged to the ward and caregivers recognize the patient's inability to perform simple activities of daily living. This weakness is typically diffuse and symmetrical with sparing of facial muscles. With critical illness polyneuropathy, an axonal polyneuropathy affecting both sensory and motor nerves, the weakness may be distal with distal sensory deficits and normal deep tendon reflexes. With critical illness myopathy, which represents a spectrum of muscle pathology, the weakness may be proximal, with decreased or absent reflexes, and no sensory deficits.[32] Critical illness polyneuropathy and myopathy commonly coexist giving rise to a complex clinical presentation. With demyelinating polyneuropathy, patients may have an ascending pattern of weakness preceding ICU admission with cranial nerve involvement, decreased or absent reflexes, and sensory abnormalities.[19]

Details of patient evaluation have been described elsewhere,[18,19] but include serial clinical examination of muscle strength with electrophysiological testing and possibly muscle biopsy in patients with severe and/or persistent deficits. It is important to recognize that this testing will reveal abnormalities that may otherwise be undetected by clinical examination. However, the functional significance of these abnormalities and the value of routine testing in clinical practice remain controversial.[20,33]

Therapy: A Paradigm Shift to Reduce Heavy Sedation and Bed Rest in the ICU

During an ICU stay, some patients may be deeply sedated with continuous infusions of sedatives and narcotics.[31] In this setting, defining an adequate level of patient sedation is difficult. Adequate sedation involves balancing the need for patient comfort, cardiopulmonary stability, ventilator synchrony, and safety (eg, prevention of accidental removal of medical devices), which may most easily be ensured with deep sedation compared with a greater degree of patient wakefulness with lighter sedation. Lighter sedation is associated with an improved ability to perform neurological evaluation (and fewer associated diagnostic tests), substantially decreased duration of mechanical ventilation and ICU stay, and potentially reduced posttraumatic stress disorder symptoms in the months following hospital discharge.[34-36]

In the ICU, patients also frequently receive corticosteroids, which may be associated with ICU-acquired weakness.[9,37] Moreover, in some settings, mechanically ventilated patients may infrequently receive physical therapy and occupational therapy. For example, in the usual care group within a single-center study of mobility therapy, only 6% of 135 mechanically ventilated patients received physical therapy in the ICU.[38] While in another study of 150 patients with acute lung injury from 11 ICUs in 3 teaching hospitals, only 27% of patients ever received physical therapy in the ICU with therapy occurring on only 6% of all ICU days.[39] Finally, a study of 20 physiologically stable patients with an ICU stay of 5 to 15 days in an academic hospital revealed that therapeutic activity beyond turning and range of motion was rare and that physical therapy was involved in less than 25% of activities.[40] A European task force on physical therapy for critically ill patients reflected similar findings in stating, "Critically ill patients are often viewed as 'too sick' to tolerate physical activity . . . and their immobilization is frequently 'inevitably' prolonged."[41]

Under this ICU course, as patients appear ready for liberation from mechanical ventilation, sedation is then reduced and patients are frequently extubated after eventual awakening. Thereafter, they are discharged from the

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Figure. Early Mobility of a Mechanically Ventilated Patient With an Oral Endotracheal Tube in the Intensive Care Unit

Mr E, a 56-year-old man with severe chronic obstructive pulmonary disease and acute renal failure, ambulating on day 4 after admission to the medical intensive care unit while receiving mechanical ventilation via an oral endotracheal tube.

ICU. Treatment with physical therapy and occupational therapy may only occur after sedation is lightened, after extubation, or once a patient is discharged from the ICU. At hospital discharge, patients also may be assessed by a physical medicine and rehabilitation physician regarding discharge to an acute rehabilitation facility where the patient would receive further care directed at regaining muscle strength and physical function.

With an ICU care strategy that includes an early focus on improving patient recovery and subsequent outcomes, aspects of physical medicine and rehabilitation are introduced within days of ICU admission. This approach includes minimization of heavy sedation (ie, aiming for target sedation levels that permit greater wakefulness, daily interruption of sedation, and use of as-needed bolus administration of sedation rather than continuous infusions[31,34,36]); increasing attention to potential ICU risk factors for weakness (eg, corticosteroids[37] and hyperglycemia[42]); consultations in the ICU for occupational therapy, physical therapy, speech language pathology, and with a physical medicine and rehabilitation physician; and increasing neurology consultation and investigation (eg, electrophysiological studies), as necessary, for patients with significant or prolonged weakness. Although clinical judgment is required when deciding to initiate early physical medicine and rehabilitation in ICU patients, some general considerations include: (1) responsiveness to stimulation (ie, not comatose), (2) respiratory stability (eg, stable oxygen saturation, fraction of inspired oxygen $\leq$0.60, and positive end-expiratory pressure $\leq$10 cm H_2O), (3) cardiovascular stability (eg, no active cardiac ischemia, hypotension, or increasing infusion of vasopressor medication), and (4) absence of an unstable fracture (eg, cervical spine).[38,43,44] Through this approach, some patients may be awake, comfortable, and ambulating in the ICU despite the requirement for mechanical ventilation and other ICU life support therapies. Such an approach may help address difficulties associated with bed rest, but cannot necessarily address all of the multiple factors contributing to neuromuscular weakness.

Evidence Supporting Rehabilitation in the ICU Setting

Among patients with chronic pulmonary conditions or long-term mechanical ventilation, prior studies have demonstrated these important points: (1) rehabilitation therapy helps patients regain their ability to ambulate and conduct activities of daily living and (2) higher-intensity rehabilitation may lead to greater benefit.[45-47] However, studies supporting the early onset of rehabilitation in the acute ICU setting are relatively new. The first published report is an uncontrolled study of routine multidisciplinary, twice daily, rehabilitation therapy in the ICU provided to 103 mechanically ventilated patients. This research demonstrated that activity, including sitting and ambulation, is feasible and safe in mechanically ventilated patients with an endotracheal tube.[43] Moreover, this study demonstrated benefit with 69% of these ICU patients ambulating more than 100 ft (30 m) by ICU discharge with a mean distance walked of 212 ft (65 m). Similar findings regarding safety and feasibility also have been described by others,[44,48] including a subsequent larger study that compared early mobility with a usual care control group,[38] which also found that early mobility patients were out of bed earlier (5 vs 11 days; $P<.001$) with a shorter length of stay in the ICU (5.5 vs 6.9 days; $P=.03$) and the hospital (11.2 vs 14.5 days; $P=.006$). Minimizing sedation and changing ICU culture to focus on recovery and rehabilitation issues are key success factors for early mobilization in the ICU.[49,50] Despite these positive findings, this existing evidence is still preliminary without the support

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of any large, multicenter, randomized controlled trials to comprehensively evaluate safety and the short-term and long-term benefits.

Experience With Early Mobility in the Johns Hopkins Hospital

Analysis of data for the Johns Hopkins Hospital medical intensive care unit (MICU) study site within a multisite prospective cohort study of patients with acute lung injury and ARDS[39] confirmed anecdotal evidence of the need for significant improvement in the area of physical medicine and rehabilitation. Specifically, only 17% and 20% of patients received physical therapy and occupational therapy, respectively, at any point during their entire MICU stay. Furthermore, these patients received any level of activity beyond bed rest in only 11% of the 2470 ICU days observed in this study.

As a result of these observations, a multidisciplinary quality-improvement project was undertaken to adopt a new paradigm of care to improve physical medicine and rehabilitation in the Johns Hopkins Hospital MICU. This project included an assessment of barriers to physical medicine and rehabilitation through review of existing practices in the MICU and consultation with all members of the multidisciplinary clinical team in the MICU and the departments of physical medicine and rehabilitation and neurology.

Based on this assessment, several changes occurred: (1) modification of the computerized order entry system to discontinue bed rest as the default activity level with MICU admission orders, (2) creation and promotion of simple guidelines for consultation with the physical and occupational therapists and physical medicine and rehabilitation and neurology physicians, and (3) additional multidisciplinary training and education for all staff in the MICU and physical medicine and rehabilitation clinicians regarding reducing heavy sedation and rehabilitation issues unique to ICU patients. These changes were implemented with the ongoing support of individual champions and the overall leaders of each clinical discipline within the MICU and physical medicine and rehabilitation department.

The patient case study, Mr E, was admitted to the Johns Hopkins Hospital MICU after initiation of the quality-improvement project and is a good example of our progress. Specifically, despite an endotracheal tube and need for mechanical ventilation, Mr E was awake, comfortable, and actively participating in rehabilitation therapy. The photo of Mr E walking in the MICU hallway was taken 4 days after MICU admission for intubation and mechanical ventilation (FIGURE). While ambulating, with the assistance of a walker, under the close supervision of physical and respiratory therapists, this photo illustrates that Mr E had (1) continuous blood pressure monitoring via a left radial arterial line, (2) continuous heart rate and rhythm monitoring via electrocardiogram leads and a portable cardiac monitor, (3) continuous pulse oximetry, (4) a urinary catheter and collection bag, (5) a peripheral intravenous line with infusion pumps providing a continuous fentanyl infusion at 25 µg/h for pain control, and (6) an oral endotracheal tube with a portable mechanical ventilator operating in synchronized intermittent mandatory ventilation mode. On the day of this photo, Mr E successfully ambulated in 3 separate physical therapy sessions for a total distance of 460 ft (140 m).

7-Month Follow-up

Mr E happily reports that his muscle strength and physical functional status have continued to improve after his discharge home. He continues to enthusiastically participate in educational activities promoting the introduction of early mobility in the ICU based on his belief that this approach helped expedite his recovery from critical illness. He has recently entered an outpatient pulmonary rehabilitation program.

CONCLUSION

Although early mobilization of critically ill patients has a historical precedent, more recently, bed rest and deep sedation have become a routine part of medical care for many mechanically ventilated patients. Given an emerging body of literature demonstrating prolonged neuromuscular complications after severe critical illness, there is growing interest in understanding the role of bed rest as a contributor to this ICU-acquired complication. Moreover, in some ICUs, medical care for mechanically ventilated patients is returning to decreased sedation and increased mobilization and rehabilitation soon after ICU admission. Preliminary investigations of this approach to ICU care provide encouraging results regarding its safety, feasibility, and potential benefits, and provide a foundation for new research and reevaluation of current medical practice for mechanically ventilated patients.

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