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SPECIAL ISSUE INSIGHT

Timing of early mobilization to optimize outcomes in mechanically ventilated ICU patients

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Weakness acquired in the intensive care unit (ICU) is a common problem in survivors of critical illness, particularly as strategies to enhance survival have increased substantially over the past two decades. This has been known from the early space flight human experience, more than 50 years ago. Here, astronauts returning to earth were noted to have extreme muscle wasting after having been in a zero gravity environment. Indeed, with modern space travel, the national aeronautics and space administration (NASA) utilizes a very sophisticated approach to exercise to ensure that astronauts no longer suffer this sort of complication. ICU patients who are motionless in bed for extended time periods suffer a similar problem. Numerous animal studies of limb immobilization and full ventilatory support have demonstrated similar findings in extremity [1] and diaphragm muscles, respectively. In 2008, Levine, et al. described marked human diaphragm atrophy in as little as 18 h of full ventilatory support in brain dead organ donors [2]. The rapidity with which neuromuscular dysfunction occurs is sobering, and combating such a formidable problem is not easy. Yet we routinely care for sedated, ventilated patients in our ICUs who suffer identical complications. Most would agree that neuromuscular and neurocognitive deconditioning is one of the most common and devastating complications seen in modern ICUs.

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In 2009, we undertook a randomized trial comparing very early mobilization to usual care [3]. This intervention implemented physical and occupational therapy an average of 1.5 days after endotracheal intubation. The study design was based upon an assumption that the intervention must occur as soon as possible to optimize chances for success. We utilized a strategy assuming that "time is muscle". Indeed, the rate limiting step to enrollment of patients in the study was the ability to obtain informed consent. Patients engaged in progressive out-of-bed physical activity and simulate functional tasks such as grooming or dressing during the interruption of sedatives [4]. The simultaneous attention to physiologic and functional recovery very early in the intensive care unit course nearly doubled the chances of functional independence on hospital discharge. This intervention dramatically reduced ICU delirium and also significantly improved ventilator free days. We noted a significantly better chance of being discharged to home rather than a non-home disposition. Schaller and colleagues noted very similar results in a randomized trial of surgical ICU patients. Specifically, they noted better functional status, shorter ICU and hospital lengths of stay, less ICU delirium and a significantly better chance of being discharged to home rather than a non-home disposition. Importantly, in this trial the time to mobilization was no later than one day after enrollment in the trial [5]. Dong, et al. noted a shorter duration of ventilation and ICU length of stay in patients subjected to early rehabilitation (i.e., less than 72 h) [6].

Despite the short-term neurocognitive and functional gains with early mobilization upon hospital discharge, many trials of ICU mobility have not demonstrated any enduring benefits in physical function in the months

after critical illness [7–10]. The RECOVER randomized clinical trial randomized patients to mobilization or usual care an average of 11 days after ICU admission [7]. Moss et al. began physical therapy in ventilated patients an average of 8 days after ventilation [8]. Wright and colleagues randomized ventilated patients to physical therapy for 30 ("standard") vs. 90 ("intensive") minutes on weekdays (Monday through Friday). Though the study design targeted physical therapy after 48 h of ventilation, patients were enrolled after a median of 4 days of ventilation and received physical rehabilitation 3 days afterwards, suggesting a 7-day delay of therapy. There were no differences noted in the two groups with regard to SF-36 physical component score, SF-36 mental component score, lengths of stay, 6-min walk test, grip strength or functional independence measures [10]. These findings lay an extremely strong foundation for the notion that timing is critical when it comes to mobilization in the ICU. After a careful look at the published literature, it seems quite clear that delayed mobilization of ICU patients imparts no discernable improvement in any important outcomes.

Early, rapid, and severe muscle wasting has been described in critically ill patients [11]. The idea of waiting a few days before starting mobilization is likely a recipe for failure of the intervention. In order for a program of very early mobilization to succeed, institutions must overcome several important barriers (Table 1). Hospital administrators may be reluctant to dedicate financial resources that allow dedicated physical and occupational therapists. However, there are numerous studies showing that shortened lengths of stay more than offset the upfront financial cost of having ICU therapy teams [12]. Another major impediment is the lack of awareness and uptake by ICU clinicians. This is true even in places where physiotherapists have been part of a multidisciplinary ICU team for many decades. We believe that the notion that ICU mobility is not effective has been driven by attention to studies that were flawed by substantial delays in initiation of mobilization. Indeed, the published data suggest that if mobilization is not begun extremely early, it is likely not worth doing it at all. To be successful, ICU teams must have leaders who direct this process, increase awareness amongst clinicians and insist on autonomy for the physical and occupational therapists in the ICU. Opportunities for the published literature to be discussed where care providers are encouraged to ask questions can be very helpful. The safety of early ICU mobility is well established and these data must be passed on to bedside providers. While extremely ill patients [e.g., severe acute respiratory distress syndrome (ARDS) with extremely high positive end-expiratory pressure (PEEP), refractory shock on multiple vasoactive drugs], may not tolerate early mobility, most ventilated ICU patients can be mobilized early. The importance of minimization of sedation to allow patients to be mobilized is imperative to ensure success. The reduction in ICU delirium noted in both the Schweickert [3] (medical ICU) and Schaller [5] (surgical ICU) studies is another under-recognized benefit of very early mobilization. Given that most interventions to reduce ICU delirium have failed, advertising this consistent benefit is another way to ensure greater clinician acceptance.

The benefits of very early mobilization are well established. To allow improved outcomes, we must ensure that awareness of the benefits is known amongst care providers. In addition, we must ensure that the necessary infrastructure is present to allow successful

Table 1 Reasons early mobility does not occur routinely

Barriers	Solutions/strategies
Lack of dedicated ICU physical and occupational therapists	Shortened length of stay [12]
Lack of awareness and uptake by clinicians	Education regarding the efficacy of mobilization when done early
	Provide autonomy to physical/occupational therapists in the ICU
	Interprofessional meetings to coordinate therapy early in the ICU
Concerns regarding safety of mobilization	Dissemination of well-established safety data of early mobility
	Adoption of safety criteria to initiate and continue a session [3, 5]
Excessive sedation	Implementation of well-established sedation practices to prevent delirium: analgosedation, avoidance of benzodiazepines, and daily awakening paired with breathing trials to minimize delirium
	Level of consciousness had no effect modification on the benefit of early mobilization; thus, early mobilization is effective regardless of degree of consciousness [13]

outcomes. Lastly, more data evaluating long-term benefit of early mobility are needed.

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Declarations

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