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WHAT'S NEW IN INTENSIVE CARE

Ten reasons why ICU patients should be mobilized early

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Introduction

Interest in early mobilization and rehabilitation in critically ill patients has grown in the last decade in response to increasing insights into long-lasting impairments experienced by many survivors. This paper describes ten reasons why patients should receive early mobilization and rehabilitation in the ICU.

Attenuates complications of bed rest

Bed rest and immobilization have significant negative effects on the musculoskeletal system, with alterations in peripheral muscle architecture, contractility, aerobic capacity, and insulin resistance [1]. Moreover, bed rest is associated with changes in the balance of systemic pro- and anti-inflammatory mediators and micro-vascular dysfunction [1]. In the setting of bed rest and critical illness, muscle wasting occurs early and rapidly with reductions of up to 30 % over the first 10 days [2]. Muscle quality, measured using ultrasonography, quickly deteriorates, with concomitant poor strength and function [2]. The combination of critical illness and bed rest may result in greater muscle loss compared with bed rest alone, due to potential synergistic effects of inflammation, sedation, corticosteroids, and neuromuscular blocking agents [1]. Notably, the duration of bed rest in the ICU was the single risk factor most consistently associated with muscle weakness in 220 ARDS survivors longitudinally followed for 2 years [3].

Addresses sequelae of ICU-acquired weakness (ICUAW)

ICUAW may be present in 25–50 % of patients, and is associated with worse long-term survival, physical function and health-related quality of life [3, 4]. Intervening with early mobilization and rehabilitation may improve muscle weakness to improve patient-centered outcomes after ICU discharge [5, 6] (Table 1).

Perceived barriers are modifiable

Patient, environment, cultural and process-related issues are major categories of barriers to implementation [7]. However, there are a wealth of strategies successfully implemented to overcome such barriers, including establishing safety criteria, identifying interdisciplinary 'champions,' and facilitating interdisciplinary communication and roles [7]. Addressing these barriers will ultimately further improve feasibility of implementation (see below).

Implementation is feasible

There is a large literature base describing successful implementation of early mobilization and rehabilitation as part of routine clinical practice. One early study demonstrated that a majority of mechanically ventilated patients walked >100 feet (c. 30 m) at ICU discharge after implementing mobility activities [8].

Promotes reduction of sedation

Early deep sedation can delay extubation and may negatively affect neuropsychiatric outcomes. Prioritizing early mobility may encourage ICUs to move away from deep sedation by providing additional rationale for changing practice. Indeed, reducing sedation and providing mobility as part of a bundle of care demonstrated a halving of the odds of delirium and doubling the odds of patients being mobilized [9].

It is safe

Across five published trials of ICU-based mobilization and rehabilitation, with >700 patients and >3000 treatments, only five potential safety events were reported [6,

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Table 1 Summary of selected controlled clinical trials of rehabilitation interventions in the intensive care unit[a]

Study, and sample size	Study type and setting	Intervention and timing of onset	Control	Selected results (intervention vs. control)
Trials with difference in physical outcomes				
Morris et al. [15] $n = 330$	Quasi-randomized controlled trial, single medical ICU in USA	Multidisciplinary mobility team started within 48 h of MV 3×/day; advanced per protocol until ICU discharge	Usual care PT	Primary outcome: Proportion of patients receiving PT intervention in ICU: 91 vs. 13 %, $P \leq 0.001$ Secondary outcomes: Hospital length of stay: mean 11 vs. 15 days, $P = 0.006$ ICU length of stay: mean 6 vs. 7 days, $P = 0.025$ Days to first out of bed: mean 5 vs. 11 days, $P < 0.001$ Mechanical ventilation duration: mean 8.8 vs. 10.2 days, $P = 0.163$
Schweickert et al. [10] $n = 104$	RCT, medical ICUs in 2 hospitals in USA	PT/OT intervention started at median of 1.5 days after MV until hospital discharge; PT/OT median duration of 19 min/day during MV	Usual care PT/OT started at median of 7.4 days after MV; PT/OT median duration of 0 min/day during MV	Primary outcome: Return to independent function at hospital discharge: 59 vs. 35 %, $P = 0.02$ Secondary outcomes: Proportion of time in ICU with delirium: 33 vs. 57 %, $P = 0.02$ Mechanical ventilation duration: median 3.4 vs. 6.1 days, $P = 0.02$ ICU length of stay: median 5.9 vs. 7.9 days, $P = 0.08$ Hospital length of stay: median 13.5 vs. 12.9 days, $P = 0.93$
Burtin et al. [6] $n = 90$	RCT, single medical-surgical ICU in Belgium	In-bed cycle ergometry started at mean of 14 days after admission, plus usual care PT; cycling was 20 min/day until ICU discharge	Usual care PT 5 days/week	Primary outcome: 6MWD at hospital discharge: mean 196 vs. 143 m, $P < 0.05$ Secondary outcomes: SF-36 PF at hospital discharge: mean 21 vs. 15, $P < 0.01$ Quadriceps force at hospital discharge: mean 2.4 vs. 2.0 N kg^{-1}, $P < 0.05$ ICU length of stay: median 25 vs. 24 days, $P = 0.14$ Hospital length of stay: median 36 vs. 40 days, $P = 0.1$
Routsi et al. [5] $n = 140$	RCT, single medical-surgical ICU in Greece	NMES started on second day of admission until ICU discharge; NMES was 55 min/day, 7 days/week	No NMES	Primary outcome: Proportion of patients with ICUAW: 13 vs. 39 %, $P = 0.04$ Secondary outcomes: Muscle strength (MRC sumscore): median 58 vs. 52, $P = 0.04$ Mechanical ventilation duration: median 7 vs. 10 days, $P = 0.07$ ICU length of stay: mean 14 vs. 22 days, $P = 0.11$

Table 1 continued

Study, and sample size	Study type and setting	Intervention and timing of onset	Control	Selected results (intervention vs. control)
Morris et al. [13] $n = 300$	RCT, single medical ICU in USA	Structured rehabilitation therapy 3× daily, 7 days/week until hospital discharge, with active therapy started at median of 3 days after enrollment (with ≤80 h from MV to enrollment)	Usual care PT started at median of 7 days after enrollment (with ≤80 h from MV to enrollment)	Primary outcome: Hospital length of stay: median 10.0 vs. 10.0 days, $P = 0.41$ Secondary outcomes: Ventilator-free days: median 24 vs. 24, $P = 0.59$ ICU length of stay: median 7.5 vs. 8.0 days, $P = 0.68$ SPPB at 2 and 6 mo.: mean 8.7 vs. 7.8, $P = 0.05$ and 9.0 vs 8.0, $P = 0.04$ SF-36 PF at 2 and 6 mo.: 47 vs 43, $P = 0.29$ and 56 vs. 44, $P = 0.001$
Trials without differences in physical outcomes:				
Denehy et al. [11] $n = 150$	RCT, single medical-surgical ICU in Australia	PT-based rehabilitation 15 min 1× or 2× daily, started at mean of 7 days after ICU admission and continued on ward and as out-patient	Usual care PT, available 7 days/week	Primary outcome: 6MWD at 12 mo.: mean 434 vs. 410 m, $P = 0.88$ Secondary outcomes: Mechanical ventilation duration: median 4 vs. 4 days, NS ICU length of stay: median 8 vs. 7 days, NS Hospital length of stay: median 24 vs. 20 days, NS Timed Up and Go test at 12 mo.: mean 10 vs. 14 s, $P = 0.22$ SF-36 PF at 12 mo.: mean 41 vs. 44, $P = 0.54$ Rate of change in 6MWD to 12 mo.: mean difference[b] 73 m, $P = 0.049$
Moss et al. [12] $n = 120$	RCT, ICUs in 5 hospitals in USA	PT intervention 7 days/week in ICU and ward, with mean duration of 31 min in ICU, starting at median of 8 days after MV	PT intervention 3 days/week in ICU and ward, with mean duration of 21 min in ICU	Primary outcome: PFP-10 score at 1 mo.: mean 20 vs. 21, $P = 0.73$ Secondary outcomes: ICU length of stay: median 15 vs. 16 days, $P = 0.69$ SF-36 PF at 1 mo.: median 35 vs. 50, $P = 0.15$ Timed Up and Go test at 1 mo.: mean 15.6 vs.15.2 s, $P = 0.9$

NMES neuromuscular electrical stimulation, *ICU* intensive care unit, *ICUAW* intensive care unit-acquired weakness, *MV* mechanical ventilation, *MICU* medical intensive care unit, *mo.* months, *MRC* medical research council, *NS* not significant, *OT* occupational therapy, *PFP-10* physical function performance test, *PT* physical therapy, *RCT* randomized controlled trial, *SF-36 PF* medical outcomes survey short form-36 physical function domain score, *6MWD* 6-minute walk distance, *SPPB* short physical performance battery

[a] For presentation in this table, trials were selected to include those with the largest sample sizes

[b] Difference in rate of change in 6MWD between intervention versus control group

10–13]. Moreover, as part of routine clinical practice, a single-center study of >1100 patients receiving >5200 treatments reported 34 potential safety events (0.6 %), with only 4 (0.07 %) requiring treatment [14].

Promotes improved functional outcomes with early start

There are at least nine published controlled trials evaluating the efficacy of ICU-based mobility and rehabilitation to improve functional outcomes (larger-sized trials summarized in Table 1). Results for functional outcomes from these trials are conflicting. All four trials with early intervention (starting within 1–4 days after ICU admission) demonstrated significant differences in physical outcomes across variable time points; [5, 10, 13, 15] albeit in two of these trials [13, 15] physical function was a secondary outcome. On the other hand, two [11, 12] of the three trials [6, 11, 12] with later intervention (starting at 7–14 days) did not demonstrate significant differences in physical function, their primary outcome. Notably, these two "negative" trials [11, 12] also had control groups that received rehabilitation at a much greater intensity than reported in international point prevalence studies and in the "usual care" control groups of trials demonstrating differences in functional outcomes (Table 1).

May improve delirium

Delirium in the ICU and post-ICU cognitive impairment are very common. Research in both healthy and diseased human subjects suggests that exercise improves neuropsychiatric outcomes [16]. A small case–control study of early functional electrical stimulation-assisted cycling demonstrated a 62 % absolute decrease in delirium incidence ($p = 0.042$) [17], and a pre-post study of a bundled sedation and mobility intervention halved the odds of delirium [9]. Moreover, a randomized controlled trial (RCT) demonstrated that ICU-based early rehabilitation reduced the incidence of delirium by 50 % in the setting of daily sedation interruption [10]; however, similar results were not demonstrated in a more recent RCT that did not include any sedation protocol with its rehabilitation intervention [13].

New technologies expand opportunities

Use of existing technologies within the ICU setting offer feasible approaches to early onset of mobilization and rehabilitation. For instance, neuromuscular electrical stimulation, bedside cycle ergometry, and these two interventions combined (i.e., functional electrical stimulation-assisted cycling) can be instituted early and provide muscle strength training for patients who are either sedated or awake, and may help preserve muscle architecture and improve strength and function [18]. Other innovative strategies include new hospital beds with built-in tilt-table functionality or easy egress to walking, and interactive video games to provide both physical and cognitive rehabilitation.

May reduce overall resource utilization

The effect of early mobilization and rehabilitation on length of stay has conflicting results from trials to date (Table 1). In one trial, there was reduced hospital length of stay along with decreased 1-year mortality and re-admissions [19], but another trial, at the same study site, found no difference [13]. Based on earlier data, a conservative financial model projected net cost savings of early rehabilitation programs within the American healthcare setting [20]; however, further analyses are warranted.

Conclusion

Only 8 years have passed since publication of the first controlled trial of early mobilization and rehabilitation in the ICU. The field is rapidly evolving with several multi-site RCTs ongoing around the world. Many questions remain, including selection of the type, duration, intensity and frequency of interventions; addressing concomitant sedation issues; determining if certain patient sub-groups have greater benefit; and determining which outcome measures and time points are most appropriate to evaluate. Moreover, more research is needed to understand the effect of critical illness and rehabilitation interventions on muscle biology. Greater precision in terminology related to physiotherapy, mobility, rehabilitation and exercise interventions, and in the definition of "early" intervention, are important to more accurately understand the effects of such interventions. These 10 reasons provide support for continued thoughtful implementation and rigorous evaluation of early mobilization and rehabilitation in the ICU with a goal of improving the ICU survivorship experience.

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Compliance with ethical standards

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest related to this manuscript.

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