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Physical rehabilitation in the ICU

Understanding the evidence

Reviews the latest evidence evaluating physical rehabilitation in the intensive care unit setting and future directions for the field.

Survivors of critical illness frequently experience poor physical outcomes, including persistent impairments in muscle strength, exercise capacity and physical function (Pfoh et al. 2016; Herridge et al. 2011; Dinglas et al. 2017; Fan et al. 2014b). In this article, we review these impairments and recent clinical trials evaluating physical rehabilitation during critical illness as a potential means to improve these outcomes, and conclude with considerations for future studies in the field (**Figure 1**).

Background: what is intensive care unit (ICU)-acquired weakness?

ICU-acquired weakness (ICUAW) is a syndrome of diffuse and symmetric muscle weakness for which no cause other than critical illness can be found (Stevens et al. 2009). Weakness is defined based on physical examination of muscle strength, in an alert and cooperative patient, using the Medical Research Council (MRC) scale. A MRC sum score of <48 (range: 0-60, maximum = 60) is consistent with ICUAW.

Muscle weakness consistent with ICUAW occurs in 11% of all patients admitted to an ICU for ≥1 day (Nanas et al. 2008), with a higher prevalence of 26-65% in patients mechanically ventilated for ≥5 days (Ali et al. 2008; Sharshar et al. 2009; Dinglas et al. 2017). Loss of muscle mass occurs quickly during critical illness. Compared to the day of ICU admission, cross-sectional area of the rectus femoris muscle decreased by 18% at day 10, with necrosis seen in 54% of muscle biopsies (Puthucheary et al. 2013).

Patients with ICUAW experience worse in-hospital and post-hospitalisation outcomes. Among patients requiring mechanical ventilation for ≥5 days, ICUAW is associated with a 2-fold increase in duration of mechanical ventilation (De Jonghe et al. 2002; Ali et al. 2008), and a 2- to 5-fold increased hospital mortality (Sharshar et al. 2009; Ali et al. 2008). One-year mortality almost doubled in a propensity-matched analysis of patients with vs. without ICUAW (30.6% vs. 17.2%, p = 0.015) (Hermans et al. 2014). Two years after surviving ICU admission for acute respiratory distress syndrome (ARDS), patients with ICUAW achieved only 40% of predicted 6-minute walk distance vs. 60% in those without ICUAW (p <0.01) (Fan et al. 2014b). In the same cohort, patients with vs. without ICUAW demonstrated decreased quality of life (QOL) two years after ARDS (30% vs. 70% of population normative scores on the Short Form 36 Health Survey (SF-36) physical function subscale, p < 0.001) (Fan et al. 2014b). Post-discharge survival over 5 years after ARDS was significantly worse in patients with ICUAW (Dinglas et al. 2017).

Pathology

ICUAW encompasses a variety of muscle and nerve disorders, which may overlap, including critical illness polyneuropathy (CIP), critical illness myopathy (CIM) and disuse atrophy (Stevens et al. 2009). CIP is defined as ICUAW with electrophysiological evidence of a sensorimotor axonal polyneuropathy; CIM is ICUAW with myopathic features on muscle biopsy or electromyography (EMG, recorded during voluntary muscle contraction). CIP and CIM frequently coexist, given common risk factors and potential mediators (Stevens et al. 2009). Pathophysiologically, CIP and CIM are associated with increased inflammatory markers, and microcirculatory and metabolic impairments that are also associated with multi-organ dysfunction syndrome (Batt et al. 2013; Witteveen et al. 2017).

Risk factors

Multiple studies have evaluated patient- and ICU-related risk factors for ICUAW. Older age, immobility, sedation, sepsis, multi-organ failure, hyperglycaemia and mechanical ventilation are consistently reported risk factors for ICUAW (Fan et al. 2014a; Puthucheary et al. 2012; Hermans and Van den Berghe 2015; de Jonghe et al. 2009). The most readily modifiable risk factors are immobility, sedation and hyperglycaemia. Steroids and neuromuscular blocking agents have been reported as risk factors (Hermans and Van den Berghe 2015; Needham et al. 2014), but a causal association is not certain (Puthucheary et al. 2012), given that immobilisation and sedation are confounders in most analyses (deBacker et al. 2017; Fan et al. 2014b). While difficult to evaluate in ICU patients, pre-ICU physical status appears to be an important factor for ICUAW and should be considered when evaluating a patient's risk for ICUAW (Batt et al. 2013; Latronico et al. 2017; Puthucheary and Denehy, 2015).

There is emerging evidence demonstrating the benefit of earlier vs. later initiation of rehabilitation in the ICU

Evidence: clinical trials evaluating physical rehabilitation in the ICU

Strength and physical function

The most direct effects of physical rehabilitation in the ICU may be on strength and physical functioning. A recent meta-analysis reported a significant improvement in muscle strength, measured by the MRC sum score, at ICU discharge (pooled mean difference 8.6, 95% CI 1.4-15.9, p = 0.02) and increased probability of walking without assistance at hospital discharge (OR 2.1, 95% CI 1.2-3.8, p=0.01) in rehabilitation intervention vs. control groups (Tipping et al. 2017). Growing evidence suggests that these improvements in strength and physical function may be greater when rehabilitation is initiated earlier. For instance, a randomised controlled trial (RCT) of physical and occupational therapy (PT, OT) interventions, started at a median of 1.5 days after intubation, vs. usual care (with PT and OT started at a median of 7.4 days after intubation) significantly increased return to independent functional status and walking at hospital discharge (59% vs. 35%, p = 0.02) (Schweickert et al. 2009). Similarly, two additional trials of early goal-directed mobilisation vs. usual care reported a doubling of the proportion of patients walking by ICU discharge (Hodgson et al. 2016; Schaller et al. 2016). By contrast, a RCT of more vs. less intensive PT interventions, beginning a median of 8 days after intubation, found no difference in functional status at 28 days (Moss et al. 2015).

Delirium

Several randomised trials have demonstrated an improvement in delirium with rehabilitation in the ICU. Early intervention by PT and OT, delivered during daily sedation interruption, resulted in a 50% decrease in delirium duration compared to very similar sedation (i.e., daily sedation interruption) with usual care rehabilitation therapy (Schweickert et al. 2009). ICU delirium-free days by day 28 increased by 3 days in patients managed with early, goal-directed mobilisation vs. usual care (Schaller et al. 2016). Notably, there was no difference in delirium incidence or duration in a RCT of standardised rehabilitation therapy vs. usual care where there was no sedation protocol and sedation levels that commonly prohibited active physical therapy interventions, which may have contributed to the lack of benefit (Morris et al. 2016). A RCT evaluating interventions led by OT (without additional PT involvement) vs. usual care, reported a dramatic decrease in delirium incidence from 20% to 3% in non-mechanically ventilated patients (Álvarez et al. 2017). Finally, pre-post evaluations of quality improvement bundles, including combined sedation and rehabilitation interventions, have resulted in marked reductions in delirium, although it is impossible to isolate the effect of the rehabilitation component in these studies (Balas et al. 2014; Needham and Korupolu 2010; Smith and Grami 2016).

Duration of mechanical ventilation and length of stay

In a recent systematic review, 3 of 11 RCTs reported significant 1.7-5.8 day decreases in duration of mechanical ventilation (Schweickert et al. 2009; Dong et al. 2016; Dong et al. 2014). Of 13 studies that evaluated ICU length of stay, 10 reported decreases (Tipping et al. 2017), but only 2 reported data that were not potentially confounded by mortality. These studies both found significant reductions of 2.5-5.1 ICU days in intervention vs. control groups ($p < 0.05$) (Yosef-Brauner et al. 2015; Dong et al. 2014).

Mortality and post-discharge status

There is no difference in mortality at ICU discharge, hospital discharge, or 6-month follow-up in existing RCTs. However, "days alive and out of the hospital at 6 months" were significantly greater with rehabilitation vs. standard care in a recent meta-analysis (mean difference 9.63 days, 95% CI 1.68–17.57, p=0.02) (Tipping et al. 2017).

Quality of life

Physical function and role physical are 2 domains of the SF-36 QOL survey. No differences were seen in these domains at 6 months after ICU admission, although differences were seen in patient subgroups. Early rehabilitation (within

Physical Rehabilitation in the ICU

Addresses ICU-Acquired Weakness (ICUAW):
A syndrome of diffuse and symmetric weakness in ICU patients for which no cause other than critical illness can be found

Importance
Occurs in 26-65% of patients with MV ≥5 days

Associated with
↑Duration of MV
↑Mortality
↓Physical Function
↓Quality of life

Risk Factors
Age
Immobility
Sedation
Sepsis
Multi-organ failure
Hyperglycaemia
Mechanical ventilation

Outcomes improved with physical rehabilitation in the ICU

In hospital:
↑Strength
↑Independent walking

Post-Hospitalisation:
↑Days alive & out of hospital

Potential additional benefits:
↓Delirium
↓Duration of MV
↓Length of stay
↑Quality of life

Abbreviations ICU = Intensive Care Unit; MV=Mechanical Ventilation

Figure 1. Summary of evidence on the importance and outcomes of physical rehabilitation in the ICU

3 days of ICU admission, 1 study) vs. control group increased the SF-36 physical function domain score (mean difference 22 points, p = 0.04) (Kayambu et al. 2013); late rehabilitation (2 studies) vs. control groups was not different (Tipping et al. 2017). The SF-36 role physical domain improved with high-dose (>30 minutes active rehabilitation daily, 2 studies) vs. control groups (mean difference 31 points, p = 0.001); low-dose rehabilitation (1 study) vs. control group was not different (Tipping et al. 2017).

Safety

Physical rehabilitation of critically ill patients (**Figure 2**) is safe (Tipping et al. 2017; Nydahl et al. 2017). A large systematic review of 22,351 mobilisation sessions delivered in 7,546 ICU patients, from a combination of observational and clinical trials, demonstrated a rare frequency of events. Potential safety events, defined as a clinical deterioration or event exceeding a study's safety limit, occurred in only 2.6% of sessions. Events of consequence, defined as being events associated with cessation of a mobility session, adverse health consequence or requirement of additional therapy, occurred in only 0.6% of sessions. Most potential safety events involved a haemodynamic change or oxygen desaturation that resolved with pause or cessation of mobility. Notably, removal of medical devices and falls were rare, including dysfunction or removal of an intravascular catheter (0.2% of sessions), endotracheal tube removal (0.01%) and falls (0.07%) (Nydahl et al. 2017).

Figure 2. Mechanically-ventilated patient ambulating in the intensive care unit

Future directions

The most pressing questions for consideration in future studies in the field include the optimal type and dose of rehabilitation interventions, timing of initiation of intervention and ICU patient sub-populations (Denehy et al. 2017). While PTs may mobilise patients to a higher level than nurses (Garzon-Serrano et al. 2011), nurses can provide clinically beneficial mobility interventions, as clearly demonstrated in a recent RCT (Schaller et al. 2016). There are many types of interventions to be considered in future studies, including functional mobility, strengthening and use of relevant technology and equipment (e.g., in-bed cycle ergometry, neuromuscular electrical stimulation, tilt tables, interactive video games, hydrotherapy), along with consideration of potentially synergistic interventions with rehabilitation, such as nutritional supplementation (Needham et al. 2009; Sommers et al. 2017; Arabi et al. 2017; Heyland et al. 2015).

There is emerging evidence demonstrating the benefit of earlier vs. later initiation of rehabilitation in the ICU, which should be considered when designing future trials and implementing rehabilitation as part of clinical practice in the ICU. Most studies have had broad eligibility criteria, but it is possible that patients' pre-ICU baseline status (e.g., frailty and comorbidity) or ICU-based diagnosis (e.g., sepsis) may better identify patients who are most likely to benefit from rehabilitation (Puthucheary and Denehy 2015).

Finally, more fully understanding the effects of ICU-based rehabilitation is limited by heterogeneity in reporting among the published reports. Future studies should adopt standardised reporting methods of intervention, potential safety events and outcome measures, including separately reporting outcomes for survivors and non-survivors where appropriate (Hoffmann et al. 2014; Slade et al. 2016; Connolly et al. 2017; Needham et al. 2017).

Conclusions

Muscle wasting and weakness commonly develops within days of ICU admission, with effects on survival and physical functioning lasting for years post-discharge. Early-onset physical rehabilitation is a safe intervention in ICU patients that, based on existing RCTs, improves strength and physical functioning, and may improve delirium in the ICU as well as in-hospital and post-hospitalisation healthcare resource utilisation. ■

Conflict of interest

Dale M. Needham is a principal investigator on a NIH-funded multi-site randomised trial evaluating nutrition and exercise in acute respiratory failure and, related to this trial, is currently in receipt of an unrestricted research grant and donated amino acid product from Baxter Healthcare Corporation and an equipment loan from Reck Medical Device. The other authors declare that they have no conflict of interest.

Abbreviations

ARDS acute respiratory distress syndrome
CIM critical illness myopathy
CIP critical illness polyneuropathy
EMG electromyography
ICU intensive care unit
ICUAW intensive care unit-acquired weakness
MRC Medical Research Council
OT occupational therapy
PT physical therapy
QOL quality of life
RCT randomised controlled trial
SF-36 Short Form 36 Health Survey

References

For full references, please email editorial@icu management.org or visit https://iii.hm/ddw