Physical rehabilitation and critical illness

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Abstract

Survivors of critical illness suffer a range of physical, psychological and social problems known together as the post-ICU syndrome. Physical weakness is common, long lasting, and interferes with quality of life for many ICU survivors. Physical weakness observed close to the time of ICU discharge is likely be caused by the disordered physiology and immobility associated with critical illness. These factors may be less important in the long term, where pre-existing frailty may be more important. A large number of trials have tested physical interventions (exercise, passive and active mobilization, and neuromuscular electrical stimulation) delivered during and after critical illness. At this time, the evidence suggests that early mobilization can improve important short-term outcomes (such as length of stay, duration of mechanical ventilation, functional independence and mobility), but have not been shown to affect long term outcomes. No physical intervention delivered after ICU discharge has demonstrated effectiveness. This article describes the physical problems experienced by ICU survivors, and provides an up to date review of critical care physical intervention trials.

Keywords Critical care; muscle weakness; muscular diseases; rehabilitation

Royal College of Anaesthetists CPD Matrix: 3C00

Learning objectives

After reading this article, you should be able to:

- describe the physical problems faced by ICU survivors
- outline the causes of intensive care unit acquired weakness
- describe key evidence supporting physical rehabilitation in critically ill adults

Rehabilitation requirements in ICU survivors

Survival from critical illness continues to improve but patients surviving critical illness suffer a range of adverse issues including physical, psychological, and social that define the post-intensive care syndrome (PICS). These issues are prevalent and ultimately prevent patients returning to pre-ICU levels of function and employment and can be associated with readmission to hospital soon after discharge. It is now recognized that ICU survivors have substantial rehabilitation needs, but due to the lack of integrated rehabilitation pathways (like those available to patients suffering from strokes, heart attacks, or head injuries), these needs are not routinely addressed.

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Rehabilitation can be defined as the process of returning to a normal (or as close to normal) life after a critical illness. This topic review focuses on physical rehabilitation, although readers should be aware that common psychological complications (such as depression and post-traumatic stress disorder), may prevent patients participating in physical rehabilitation, will likely compound ongoing disability, and should also be considered as part of a holistic rehabilitation package.

Physical weakness after critical illness

Physical deficits are common in survivors of critical illness. They are long lasting and are severe enough to impair quality of life. An acquired muscle weakness (intensive care unit acquired weakness [ICUAW]) is considered to be the major cause of early post-ICU functional impairment and results in delayed weaning from mechanical ventilation and increased mortality. Pre-critical illness health and function may be more important determinants of long-term physical function. The pathological processes involved in ICUAW are not consistent. The majority of patients experience muscular atrophy, termed critical illness myopathy (CIM), whereas a smaller number experience axonal damage, termed critical illness neuropathy (CIPN). In addition to structural damage, reversible impairments in ion channel transport, and mitochondrial function, contribute to weakness.

In contrast to the onset of ICUAW, our understanding of the resolution of ICUAW is less complete. It is difficult to know the true reversibility of ICUAW in the average ICU survivor and impossible to know the contribution of residual CIP and CIPMN to long-term functional deficits. It follows that the design of treatments to improve function have been based on an incomplete understanding of the natural history of ICUAW and this likely explains why the majority of interventional studies have failed to show long-term benefit. There exists a complex interplay between acute muscle atrophy, chronic poor health and short- and long-term outcomes. Rehabilitation interventions delivered to patients while they are in ICU seem to be of benefit in the short term, whereas long-term outcomes have so far been difficult to alter by interventions delivered at any point in a patient's critical illness journey.

Summary of evidence from ICU rehabilitation trials

In recent years there has been an expansion in the volume of literature evaluating rehabilitation interventions during and after intensive care. Important trials are discussed in the following sections and are summarized in Table 1. An overview of systematic reviews published in 2016 comprehensively evaluated

Key trials investigating the effects of physical rehabilitation interventions

	n	Patients	Intervention	Control	Findings
Physical interventions delivered during intensive care					
Schweickert 2009[2]	104	ICU patients ventilated <72 h	Progressive exercise and mobilization	Routine care	Higher proportion returned to independence by hospital discharge. No effect on physical outcomes
Kayambu 2015[3]	50	Septic ICU patients	Early physical rehabilitation	Routine care	No difference between groups. Underpowered.
Schaller 2017[4]	200	ICU patients ventilated <48 h	Early goal-directed mobilization directed by nominated facilitator	Routine care	Improved ICU mobilization Shortened ICU length of stay Improved functional mobility at hospital discharge
Physical interventions delivered after intensive care					
Jones 2003[5]	126	ICU patients	Ward visits, telephone calls, clinic appointments	Routine care	Positive effect on physical function score of medical outcomes study short form 36 (SF-36)
Elliot 2011[6]	195	ICU patients, ventilated >24 h	Individualized endurance and strength training, physical trainer home visits, phone calls, exercise manual	Routine care	No effect on physical function
Batterham 2014[7]	59	ICU patients 8–16 weeks after discharge	3 x 2 h cycle ergometry sessions per day	Routine care	No effect on physical outcomes, anaerobic threshold, or health-related quality of life
Walsh 2015[8]	240	ICU patients ventilated >48 h ready for ICU discharge	Hospital based complex rehabilitation involving generic rehabilitation assistant	Routine care	No effect on physical function, health-related quality of life or symptoms at 3 months
McDowall 2017[9]	60	ICU patients ventilated >96 h.	6 week individualized community based physical intervention	Routine care	No effect on self-reported physical function
Physical interventions started during ICU and continued into the in the post-ICU period					
Denehy 2013[10]	150	ICU patients with length of stay >5 days	Intensive exercises in ICU, on the ward, and after hospital discharge	Routine care	No effect on 6 min walk test, timed up and go test, or health-related quality of life
Morris 2016[11]	300	ICU patients ventilated for respiratory failure.	Protocolized rehabilitation therapy started at ICU admission and continued until hospital discharge	Routine care	No effect on length of stay, ventilator days, muscle strength, or health-related quality of life but there were possibly some small differences on physical function at 6 months

Table 1

studies of physical interventions delivered across the entire recovery period (i.e. interventions delivered at any time after the onset of critical illness). The review reported high-quality evidence that physical rehabilitation (e.g. strengthening exercises, functional activities such as lying to sitting, cycle ergometers, and electrical muscle stimulation) delivered early during critical illness are probably effective at improving some short-term outcomes (ICU length of stay, hospital length of stay, hospital mortality). The evidence for improvement in physical impairment, activity limitation and participation restriction was weaker. There was a suggestion that long-term outcomes might also be improved by early rehabilitation but the heterogeneity in the included trials made this finding tentative at best. A number of important studies have been published since the included systematic reviews were published and are discussed in the following sections.[1]

Physical interventions delivered during ICU

In 2009, Schweichert and colleagues published a trial of 104 ventilated patients in ICU testing the effect of an early mobilization intervention (<72 hours of mechanical ventilation). They found a greater proportion of patients in the intervention group returned to independent function, that they had less delirium, and a shorter period of mechanical ventilation.[2] Kayambu and colleagues recruited 50 patients to their pilot study of early physical rehabilitation in septic patients, but were underpowered to detect a difference in physical function between the two groups.[3] A large multicenter randomized controlled trial was conducted of early goal-directed mobilization provided by a mobility 'facilitator' in patients requiring mechanical ventilation in surgical ICU. In this study patients in the intervention group had shorter periods of mechanical ventilation, improved ICU mobilization and improved functional mobility at hospital discharge. However, there were more adverse events (mainly hypotension) reported in the intervention group. There was no effect on health-related quality of life 3 months after hospital discharge, or the incidence of ICUAW.[4]

Physical interventions delivered after ICU

Jones and colleagues tested a post-ICU follow up intervention that included provision of a rehabilitation self-help manual and found an improvement in physical components of health-related quality of life 6 months after ICU discharge.[5] In an 8-week home-based physical rehabilitation trial of 195 patients, Elliot and colleagues found no effect on physical function or quality of life.[6] Batterham and colleagues tested the effect of a post-ICU ward-based physical intervention that included the use of supervised cycle ergometer training for 60 minutes each day plus an additional unsupervised exercise session. They observed no improvement in anaerobic threshold, physical function or quality of life.[7] Walsh and colleagues published their RECOVER trial in 2015 which tested a complex ward-based rehabilitation intervention that included physical rehabilitation delivered by dedicated rehabilitation assistants, finding no effect on physical recovery or health-related quality of life.[8] Trials of interventions delivered after hospital discharge have had conflicting results. The REVIVE clinical trial studied the effect of a 6-week exercise programme in 60 patients discharged home after critical illness and found no effect on physical health-related quality of life.[9]

Physical interventions started during ICU and continued in the post-ICU period

Denehy and colleagues randomized 150 participants to intensive ICU and ward based exercise or standard ward care. They found no difference in physical function or health-related quality of life between groups.[10] Morris and colleagues randomized 300 adult ICU patients to a standardized daily exercise and mobilization programme initiated in ICU and continuing until hospital discharge with the primary aim of reducing hospital length of stay. Although there was no effect on length of stay, ventilator days, muscle strength, or health-related quality of life there were possibly some small differences on physical function at 6 months.[11]

Neuromuscular stimulation (NMS)

In recent years, neuromuscular electrical stimulation has emerged as a possible treatment. In an early study, Kho and colleagues noted improvements in walking distance and muscle strength when NMS was delivered during ICU.[12] Routsi went on to test the treatment in ICU of 140 patients. Although there was high attrition in this study, a reduction in patients developing ICUAW was noted.[13] Neuromuscular stimulation has not been shown to be of benefit when delivered after ICU discharge.

Conclusions and recommendations

There is convincing evidence that physical rehabilitation should be started soon after patients are admitted to ICU, and that these measures are likely to improve short term outcomes. At this time, there is little evidence to suggest that these measure improve long-term physical function, and interventions initiated after ICU, have not been shown to be of benefit so far. ◆

REFERENCES

1 Connolly B, O'Neill B, Salisbury L, et al. Physical rehabilitation interventions for adult patients during critical illness: an overview of systematic reviews [Internet]. *Thorax* 2016; **71:** 881–90 [cited 2018 Apr 3] Available from: http://www.ncbi.nlm.nih.gov/pubmed/27220357.

2 Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial [Internet]. *Lancet* 2009; **373:** 1874–82 [cited 2018 Apr 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/19446324.

3 Kayambu G, Boots R, Paratz J. Early physical rehabilitation in intensive care patients with sepsis syndromes: a pilot randomised controlled trial. [Internet]. *Intensive Care Med* 2015; **41:** 865–74. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=25851383.

4 Schaller SJ, Anstey M, Blobner M, et al. Early, goal-directed mobilisation in the surgical intensive care unit: a randomised controlled trial [Internet]. *Lancet (London, England)* 2016; **388:** 1377–88. Available from:, http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medc&NEWS=N&AN=27707496.

5 Jones C, Skirrow P, Griffiths RD, et al. Rehabilitation after critical illness: a randomized, controlled trial. [Internet]. *Crit Care Med* 2003; **31:** 2456–61. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=14530751.

6 Elliott D, McKinley S, Alison J, et al. Health-related quality of life and physical recovery after a critical illness: a multi-centre randomised controlled trial of a home-based physical rehabilitation program [Internet]. *Crit Care* 2011; **15:** R142 [cited 2018 Mar 14] Available from: http://ccforum.biomedcentral.com/articles/10.1186/cc10265.

7 Batterham AM, Bonner S, Wright J, et al. Effect of supervised aerobic exercise rehabilitation on physical fitness and quality-of-life in survivors of critical illness: an exploratory minimized controlled trial (PIX study). [Internet]. *Br J Anaesth* 2014; **113:** 130–7. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medc&NEWS=N&AN=24607602.

8 Walsh TS, Salisbury LG, Merriweather JL, et al. Increased hospital-based physical rehabilitation and information provision after intensive care unit discharge [internet]. *JAMA Intern Med* 2015; **175:** 901 [cited 2018 Mar 21] Available from: http://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2015.0822.

9 McDowell K, O'Neill B, Blackwood B, et al. Effectiveness of an exercise programme on physical function in patients discharged from hospital following critical illness: a randomised controlled trial (the REVIVE trial) [Internet]. *Thorax* 2017; vol. 72**:** 594–5. Available from:, http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medc&NEWS=N&AN=27852953.

10 Denehy L, Skinner EH, Edbrooke L, et al. Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up [Internet]**17**. 2013. Crit Care; R156. Available from:, http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med7&NEWS=N&AN=23883525.

11 Morris PE, Berry MJ, Files DC, et al. Standardized rehabilitation and hospital length of stay among patients with acute respiratory failure [internet]. *Jama* 2016; **315:** 2694. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2016.7201.

12 Kho ME, Truong AD, Zanni JM, et al. Neuromuscular electrical stimulation in mechanically ventilated patients: a randomized, sham-controlled pilot trial with blinded outcome assessment. [Internet]. *J Crit Care* 2015; **30:** 32–9. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=25307979.

13 Routsi C, Gerovasili V, Vasileiadis I, et al. Electrical muscle stimulation prevents critical illness polyneuromyopathy: a randomized parallel intervention trial [Internet]. *Crit Care* 2010; **14:** R74 [cited 2018 Jun 21] Available from: http://www.ncbi.nlm.nih.gov/pubmed/20426834.

