Early mobilization in neurocritical care patients

Monisha A. Kumar[a,b,c], Francisco G. Romero[a], and Kiruba Dharaneeswaran[a]

Purpose of review
To examine the potential benefits of early mobilization in neurocritically ill patients and to summarize the recent evidence for and against early mobilization.

Recent findings
Early ICU mobilization in medically critically ill patients may decrease ICU and hospital length of stay, increase discharge-to-home, and reduce medical costs. Whether these benefits apply to neurologically critically ill patients remains unclear, as neuro ICU patients are often excluded from trials of early mobility. Neurocritically ill patients may present with hemodynamic instability, acute hemiplegia, altered consciousness and visual field deficits which complicate mobilization, or have cerebral ischemia, which may be exacerbated when upright or active. Results of early mobilization in neurocritical care are mixed. For example, a randomized trial in acute ischemic stroke demonstrated that very early mobilization was associated with worse outcomes. However, many smaller intervention trials in neurocritical care demonstrate safety and feasibility with early mobilization, including those in patients with invasive devices, for example, external ventricular drains.

Summary
Given successes in other critically ill populations, early mobility of neurocritically ill patients may be warranted. However, caution should be exercised given the results in acute stroke trials. In addition, before routine use, the character, quality, dose, duration, and timing of early mobilization therapies requires further definition.

Keywords
critical care, early mobility, early mobilization, early rehabilitation, intensive care mobility

INTRODUCTION

Critical illness often results in long-term sequelae including ICU-acquired weakness (ICUAW), cognitive dysfunction, and poor quality of life among survivors. ICUAW, thought to be from a combination of muscle atrophy and systemic inflammation [1], may result in increased duration of mechanical ventilation [2▪,3,4▪,5], greater incidence of venous thromboembolism [6,7] and dependence on vasopressor agents [1,7,8]. Immobility in the ICU, which occurs in 25–50% of critically ill patients [9▪,10,11], is likely a critical determinant of ICUAW. ICU mobility may be one of the most important modifiable risk factors with the potential to impact long-term survival, physical functioning, and quality of life, as well as to treat pain, minimize sedation and combat delirium in the ICU.

However, whether early mobilization (defined as mobilization <72 h from ictus) [12▪] benefits neurocritically ill patients is controversial. Neurologically injured patients have a higher risk of falls, impulsivity, and altered consciousness, which makes mobilization more challenging (Table 1). Furthermore, brain injury may affect cerebral autoregulation and may render patients susceptible to cerebral ischemia with changes in head position, blood pressure or intracranial pressure (ICP). Indeed, patient transport to and from the radiology department for imaging studies has been shown to adversely affect brain metabolism [13]. Transport-related cerebral ischemia is greater in patients with more severe baseline abnormalities in brain metabolism, for example, ICP or brain oxygen. Acutely brain injured patients also may have intracranial devices that if dislodged may cause further injury. Historically, such patients were treated with

[a]Departments of Neurology, [b]Departments of Neurosurgery and [c]Departments of Anesthesiology & Critical Care, University of Pennsylvania Health System, Philadelphia, Pennsylvania, USA

Correspondence to Monisha A. Kumar, MD, Associate Professor, Departments of Neurology, Neurosurgery and Anesthesiology & Critical Care Director, Neuro ICU, Hospital of the University of Pennsylvania, University of Pennsylvania Health System, 3400 Spruce Street Philadelphia, PA 19104. Tel: +1 215 662 3396; fax: +1 215 614 1927; e-mail: Monisha.Kumar@pennmedicine.upenn.edu

Curr Opin Crit Care 2020, 26:147–154
DOI:10.1097/MCC.0000000000000709

KEY POINTS

- Early mobilization of critically ill patients has been shown in randomized clinical trials to improve functional outcomes. However, the type, dose, intensity, and frequency of early mobilization remains poorly defined.
- In medical and surgical critically ill patients, mobilization is well tolerated, even among intubated patients.
- There are potential dangers with early mobilization, especially for some neurocritical care patients, for example, acute ischemic stroke. Further research is needed to understand the impact on timing of mobilization in neurocritical care.
- Case series and small cohort studies suggest that early and progressive mobilization of neurocritically ill patients with external ventricular drains is feasible and appears to be safe.

strict bedrest to reduce device dislodgment, intracranial hemorrhage or possible infection. On the other hand, early mobilization in neurocritically ill patients may capitalize on an early and narrow window of neural plasticity and neuronal reorganization to compensate for connections lost from the injury [14]. This review will examine the evidence underlying early mobilization in neurocritically ill populations, consider new technologies for mobilization and highlight areas for further study.

GENERAL CRITICAL CARE

Bedrest has long been advocated as a treatment, albeit unproven, for critical illness. However, bedrest may delay recovery and cause harm. In medically critically ill patients, immobility has been shown to reduce lung volumes, decrease mucociliary clearance and increase the incidence of ventilator-associated pneumonia (VAP) [1,7,8].

Over the last few years, randomized controlled trials (RCTs) data suggest a benefit of early mobilization for critically ill patients. In 2009, Schweickert *et al.* [15] published the first RCT of ICU mobilization in mechanically ventilated patients. In this pivotal trial, 104 adult patients treated with mechanical ventilation for less than 72 h were randomized to early mobilization with sedation interruption or to sedation interruption without mobilization. The primary endpoint was the number of patients who achieved independent ambulation and the ability to perform six activities of daily living (ADL) at hospital discharge. Patients in the treatment arm underwent first mobilization at a mean of 1.5 (1.0–2.1) days from intubation, compared with a mean of 7.4 (6.0–10.9) days in the control group. The primary outcome was significantly greater in the treatment group (59 vs. 35% of the control group). Safety issues were similar in the two groups. All measures of mobility: out-of-bed, standing, marching in place, transferring to a chair, and walking occurred significantly earlier in the treated patients. Patients in the treatment arm also experienced less delirium and more ventilator free days over the subsequent 28 hospital days than controls. Unlike early mobilization, studies of intensive, but late-onset (>7 days after ICU admission), physical therapy initiatives, however, have not demonstrated improved outcomes [16].

Since the pivotal Schweickert *et al.*'s study [15], several other RCTs have examined mobilization in mechanically ventilated patients [2▪,3,4▪,9▪]. These trials however have enrolled relatively few patients, and have had heterogeneous design. Hence, the results have been mixed. A meta-analysis of 14 randomized and case–controlled trials ($n = 1753$)

Table 1. Population specific considerations of early mobilization in neurocritical care

Diagnosis	Time to mobilization	Consideration	Proposed solution
Ischemic stroke	>24 h	Cerebral perfusion, HOB changes	Close BP monitoring, avoid mobilization if titrating vasopressors
SAH	24–48 h after ruptured aneurysm secured	EVD dislodgement ICP elevation	Ensure EVD secure Single transient spike does not preclude mobilization
ICH	≥24 h; hemorrhage stability	Increases in BP	Monitor BP closely, may mobilize while infusing vasoactive medications
SCI	24 h postspine stabilization	Orthostatic hypotension	Close BP monitoring, avoid mobilization if titrating vasopressors
TBI	24 h after hemorrhage stable	ICP elevation	Monitor ICP closely, single transient spike does not preclude mobilization

BP, blood pressure; EVD, external ventricular drain; HOB, head of bed; ICH, intracerebral hemorrhage; ICP, intracranial pressure; SCI, spinal cord injury; SAH, subarachnoid hemorrhage; TBI, traumatic brain injury. Adapted from [36].

found that mobilization does not influence short-term or long-term mortality, but may improve muscle strength and mobility status at hospital discharge [17]. A subsequent meta-analysis that included 23 RCTs ($n = 2308$) demonstrated that early mobilization may reduce the incidence of ICUAW, increase the proportion of standing patients, increase the number of ventilator free days, increase the distance of unassisted walking, and increase home discharge [9▪]. However, heterogeneity among studies and poor quality of included studies limits generalizability and the strength of findings. In 2018, the Cochrane group identified only four high-quality RCTs ($n = 690$) of early ICU mobilization and identified a high risk of performance bias and a high rate of dropout in the included studies [18▪▪]. They noted a significant lack in the description of the type, dose, intensity, and frequency of mobilization and concluded that there was insufficient evidence to support early mobilization in the ICU.

There has been limited study of early mobilization in surgical ICU (SICU) patients, perhaps because of safety concerns (Table 2) after elective surgery. In 2016, Schaller *et al.* [19] demonstrated that early goal-directed mobilization significantly improved functional mobility and ICU length of stay (LOS) in 200 surgical ICU patients. This RCT quantitated the dose of mobilization, using the SICU optimal mobilization score (SOMS), a numerical rating scale ranging from 0, indicating no mobilization, to 4, indicating ambulation. The authors found that early mobilization significantly improved the mean achieved SOMS (2.2 in the intervention group vs. 1.5 in the control group). Early mobilization also improved the proportion of patients who were discharged directly home, despite a trend toward higher mortality and more adverse events in the intervention arm. Early mobilization was not associated with increased ventilator-free days, sedation-free days, or vasopressor-free days. However, the number of ICU-delirium free days was greater in the treatment group. This suggests that mobilization, independent of sedation, may mitigate delirium. Post-hoc analysis of this trial also showed that early, goal-directed mobilization was feasible and even may be beneficial in patients with impaired consciousness defined as Glasgow Coma Scale 8 or less on admission [20▪▪].

Table 2. Possible inclusion and exclusion criteria for mobilization among different critically ill patient populations

Organ system	Inclusion criteria	Abort criteria
Neurological	GCS > 3 Spinal stability	Reduced consciousness Lightheadedness Agitation Fall Device dislodgement
Cardiovascular	HR 60–130 bpm SBP 90–180 mmHg MAP 60–100 mmHg	Bradycardia or tachycardia Hypotension or hypertension Development of arrhythmia New chest pain Ventricular dyssynchrony
Respiratory	RPM 5–40 O_2 sat >88% FiO_2 < 60% PEEP < 10	RPM < 5 or >40 Desaturation Ventilator dyssynchrony Airway device dislodgement

FiO_2, fraction of inspired oxygen; GCS, Glasgow Coma Score; HR, heart rate; MAP, mean arterial pressure; O_2 sat, oxygen saturation; PEEP, positive end expiratory pressure; RPM, respirations per minute. Modified from [21].

NEUROCRITICAL CARE

There are several unique features in neurocritical care that reduce the potential utility of early mobilization. First, the prescription of mobilization and physical therapy to patients who are moribund, aphasic or hemiplegic is counter-intuitive. Second, some neurocritically ill patients have intracranial devices, which if dislodged, could cause significant hemorrhage or infection. Third, in neurologically ill patients, bedrest has been proposed as a therapeutic intervention and advocated as a measure to optimize cerebral hemodynamics after brain injury. For example, lying flat is thought to augment cerebral blood flow (CBF) and increase cerebral oxygenation, whereas head elevation (but bedrest) is postulated to enhance venous return from the head and hence help control ICP. Small nonrandomized studies suggest that lying flat may increase CBF [22,23] and augment cerebral oxygenation as determined by near-infrared spectroscopy [24,25]. Consequently, neurologically critically ill patients often are excluded from mobilization trials in general critical care.

To date RCTs of early mobilization in neurocritical care patients are lacking. However, support for the concept of early mobilization in neurocritical care is provided by pre and postintervention trials. One of the earliest studies to evaluate early mobilization in neurocritical care was published in 2012 [26]. In this study, a hospital-wide mobility campaign was introduced and patients treated in the 10 months before ($n = 77$) and in the 6 months ($n = 93$) after the mobility protocol was introduced were compared. The cohort included patients with subarachnoid hemorrhage (SAH, 21%), brain tumors (18%), ischemic stroke (17%), intracerebral hemorrhage (ICH, 9%), traumatic brain injury (TBI, 11%), spine injury (8%), and other illnesses (13%). Patients were evaluated daily, but time to mobilization before and after intervention was not clearly stated. Contraindications to the mobility protocol included spinal instability, acute stroke after tissue plasminogen activator or endovascular thrombectomy (<24 h), increased ICP, active resuscitation for life-threatening hemodynamic instability, spinal traction, inserted femoral sheaths, continuous renal replacement therapy, advanced modes of ventilation, and palliative care. The presence of external ventricular drains (EVDs) was not considered a contraindication. The study used a mobility algorithm (PUMP Plus), based on a validated measure from the University of Kansas, and a standardized mobility assessment, the iMove tool [27], which accords a numerical score (1–50 points) to the highest level of mobility attained during that session. The study found that participation in the hospital-wide initiative: improved mobilization; reduced ICU and hospital LOS; reduced hospital acquired infections (HAIs); and decreased restraint-days. Specifically, the mean iMove scores improved from a mean of 14.5 points preintervention to 44.7 points postintervention. Furthermore, the number of patients with an iMove score of 0 decreased from 92 (47.3%) to 27 (8.3%) after intervention. Mobilization also reduced the likelihood of HAIs. There were no recorded VAPs during the postintervention phase and although the number of catheter-associated urinary tract infections (UTIs) was similar in the two phases, catheter utilization decreased by more than 20% postintervention.

In 2015, a pre and postintervention trial described similar results [28]. Among 637 patients, 260 were in the preintervention phase and 377 were in the postintervention phase. There was a lower incidence of mechanical ventilation and a higher incidence of preadmission gait abnormalities in the postintervention group. The time to first mobilization was not described between groups, although the protocol specified that patients be evaluated for entry every 12 h. In the postintervention group, the number of patients who were weight bearing, pivoted to a chair, and/or walked, with or without assistance was double that of the preintervention group (42.7 vs. 21.2%). Hospital LOS was reduced 33% (a mean reduction of about 5 days) and ICU LOS 45% (a mean reduction of 3.5 days) in the postintervention group. In addition, there were significantly fewer blood stream infections and hospital-acquired pressure ulcers in the postintervention group. In a sub analysis of psychological profile, patients in the postintervention arm endorsed significantly less anxiety with a trend toward less depression. In multivariable analysis, after adjusting for potential confounders including mechanical ventilation and gait disturbances, higher mobility levels, ICU and hospital LOS and home discharge continued to favor intervention. The psychiatric symptoms and HAIs were not significantly different in multivariable analysis.

ACUTE ISCHEMIC STROKE

Acute ischemic stroke (AIS) may be a relative contraindication to very early mobilization (VEM; defined as mobilization <24 h from ictus hours). In these patients, the penumbra, or oligemic but not yet infarcted tissue, depends on collateral circulation. Early mobilization has the potential to reduce CBF and so could exacerbate ischemia and increase the size of the stroke. Indeed, stroke patients may be treated by lowering the head of the bed to augment CBF. By contrast current guidelines [29] recommend early mobilization to facilitate rehabilitation in hospitalized AIS patients at an intensity commensurate with anticipated benefit and tolerance. However, a precise definition of timing, dose, and duration of mobilization remains elusive [30].

This question of VEM in AIS was examined in the 'A Very Early Rehabilitation Trial for Stroke' (AVERT) study. The phase II study [31] demonstrated safety and feasibility of VEM. The phase III trial included 2000 patients [32], in 56 stroke centers across five countries with AIS or hemorrhagic stroke. Patients were randomized to VEM or standard care. Patients, outcome assessors, and investigators were blinded to treatment allocation. Ninety-two percentage of patients were mobilized within 24 h in the VEM arm compared with 59% in the standard care arm. Mortality and adverse events were similar in the two groups. However, standard care patients (50%) were more likely to have a favorable outcome (90-day modified Rankin score of 0–2, indicating a mild disability or better) than in the VEM group (46%). The authors suggested that the outcome difference may be associated with the increased frequency (median 6.5 vs. 3 times per day) and duration (median 31 vs. 10 min) rather the timing of mobility since the onset of mobilization between the groups was similar (median 18.5 vs. 22.4 h in VEM vs. standard care). However, the reasons for the observed difference in functional outcome remain unclear. Whether the results of AVERT-III can be generalized to all AIS patients is unclear as only 6% of screened patients were enrolled and VEM can be difficult to standardize across multiple sites. In addition, AVERT enrolled ICH patients, a population that may be significantly different from AIS patients.

HEMORRHAGIC STROKE

Subarachnoid hemorrhage

Bed rest is often recommended for aneurysmal SAH patients. First, bed rest is postulated to reduce the risk of rebleeding. Second, these patients often present with early global brain injury, acute cardiomyopathy, and/or neurogenic pulmonary edema. Third, bed rest often is required following an angiogram or endovascular procedure to ensure closure at the vascular puncture site. Fourth, delayed cerebral ischemia (from vasospasm) may be exacerbated by mobilization. Finally, a large number of patients require an EVD, ICP monitor or perhaps a lumbar drain. The presence of these devices is considered a relative contra-indication to mobilization. In addition, mobilization may be dangerous, for example, CSF over-drainage resulting in symptomatic intracranial hypotension may occur when using an EVD.

A few small clinical studies suggest that early mobilization is safe in SAH patients [33–36]. For example, Karic *et al.* [35] performed a prospective, interventional study in SAH patients to examine the effects of a stepwise early mobilization program (within 24 h of aneurysm repair) on complications. The following patients were excluded increased ICP (>20 mmHg), low mean arterial pressure (MAP) (<80 mmHg), evidence of symptomatic vasospasm, or radiographic/angiographic/sonographic evidence of vasospasm. The incidence of complications was similar in the early mobilization and standard care groups. In addition, there was a tendency for less frequent and less severe vasospasm in the early mobilization group. Indeed, their analysis suggested that each early mobilization step during the first 4 days following aneurysm occlusion was associated with a reduced risk of severe vasospasm of 30%. Whether conclusions about early mobilization and vasospasm can be made is uncertain as twice as many patients in the early mobilization group received intraarterial nimodipine than in the control group. The authors speculated that if early mobilization were associated with reduced vasospasm it may be considered similar to the role of head shaking and cisternal irrigation in vasospasm. At 1-year follow-up, early mobilization doubled the odds of favorable outcome among poor grade patients [33]. However, no outcome benefit was observed in the whole cohort of patients [34].

Invasive intracranial monitors and in particular EVDs are often cited as an indication for bedrest. However, Young *et al.* [37■■] recently demonstrated the safety and feasibility of transition from total bedrest, to physical therapy-driven mobilization and ultimately to a nurse-driven mobilization in SAH patients with EVDs. A strict algorithm was followed: if able to tolerate EVD clamping for 30 min, patients were mobilized with appropriate safeguards to three levels: Level 1, lift to chair; Level 2, stand and pivot; and Level 3, ambulation. They found that patients were mobilized more frequently in the nurse-driven phase of mobilization (7.1 times per ICU stay vs. 3.0). There was a trend to less tracheotomies and to shorter ICU LOS and ventilator days. In multivariable analysis, each early mobilization session increased the odds of discharge to home or in-patient rehabilitation by 3.8, independent of age and severity of illness. Other studies [38■■,39■■] have also demonstrated the success of early mobilization in patients with EVDs although usually this is reserved for patients who are awake and following commands, have adequate MAP (>80 mmHg), ICP that is controlled (<20 mmHg), and no evidence of vasospasm (e.g., Lindegaard ratio <3.0 or middle cerebral artery mean blood flow velocity <120 cm/s in patients with SAH).

Intracerebral hemorrhage

The American Stroke Association Guidelines for the acute ICH treatment recommend rehabilitation as early as possible. However, the guidelines [40] do not define the dose, intensity, or duration of mobilization. The only multicenter RCT of early (<48 h) mobilization was performed in China [41] and demonstrated that early mobilization was associated with decreased mortality, improved quality of life measures on the Short Form 36 tool, functional mobility, as defined by the Barthel index, and anxiety scores on the Self-Rating Anxiety Scale at 6 months but not at other timepoints. Bahouth *et al.* [12■] have also demonstrated the safety and feasibility of an early mobilization algorithm in ICH. Fifty-seven patients were screened daily for participation in either an active or passive mobilization pathway determined by the level of consciousness and motor function. Passive mobilization consisted of Levels 1–3 on a locally designed eight-level scale. Prealgorithm patients ($n = 28$) were compared with postalgorithm patients ($n = 29$). Baseline patient characteristics were similar. Early mobilization was safe and appeared to improve independence with ADLs and decrease hospital LOS. In addition, a nonsignificant reduction in mortality was noted in the intervention arm.

TRAUMATIC BRAIN INJURY

The role of early mobilization after TBI is only beginning to be elucidated. In general, early mobilization after severe TBI usually occurs at a least a week after injury and consists largely of passive range of motion [42]. There are several potential barriers to early mobilization in TBI, including ICP fluctuations, hematoma expansion, and a loss of cerebral autoregulation among others [36]. There is some evidence that early mobilization and a continuous chain of rehabilitation that begins with the acute phase may help severe TBI patients [43]. For example, Andelic *et al.* [43] performed a quasiexperimental study that included 61 surviving severe TBI patients at a Norwegian Level I trauma center. Early mobilization (mean time to mobilization was 12 days) was associated with better Glasgow Outcome Score-Extended (GOSE 6–8) at long-term follow-up (71 vs. 37% in the delayed rehabilitation group). The Disability Rating Scale also was enhanced in the early mobilization group. However, firm recommendations about physiotherapy and, in particular early mobilization, in the postacute phase after severe TBI remain lacking given the paucity of studies. Systemic reviews suggest that more intensive rehabilitation programs lead to earlier functional abilities [17]. Exactly what defines intensive rehabilitation is still to be fully elucidated.

Passive mobilization by tilt table devices has been proposed as a safe therapeutic option for patients with severe brain injury (Fig. 1). This device can be particularly useful in the comatose patient as it does not require patient participation. Clinical studies suggest that early upright positioning may promote arousal [44], reduce ankle contracture [45], and improve lung function [46]. Given the feasibility of tilt table passive mobilization, a current trial is underway to evaluate its use in severe TBI [47▪]. In addition, other mobility technology devices, for example, range of motion exercises, supine cycle ergometry or a treadmill with a strap system among others may help facilitate progressive mobilization in neurocritical care. A mobilization scoring system and a multidisciplinary approach with clearly defined responsibilities also is important to the success of early mobilization.

SPINAL CORD INJURY

Spinal cord injury (SCI) guidelines recommend early rehabilitation and out-of-bed activity [48]. This depends on stability of the spine which in turn is a reason advocated for early surgery after spine trauma. However, orthostatic hypotension that may be associated with loss of sympathetic tone, altered baroreceptor function, and decreased lower extremity muscle contraction among other reasons can occur after SCI. This may limit or prevent early mobilization when efforts to augment spinal cord perfusion are needed. The effects of early mobilization in SCI remain to be fully explored. Nevertheless there are several benefits and in particular immobility-related complications, for example, pneumonia, pressure ulcers, and venous thromboembolism are less frequent [36]. Retrospective studies in SCI patients demonstrate that patients who are discharged earlier to rehabilitation facilities appear to have improved functional outcomes [49]. These potential benefits of early mobilization require further study.

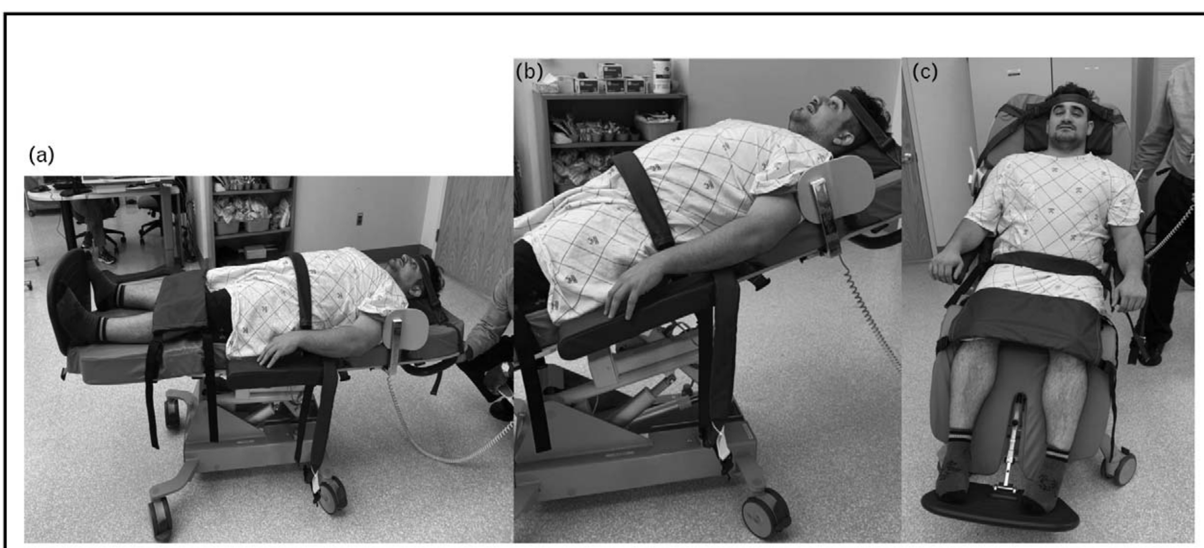

FIGURE 1. Here we can observe maneuvers that can safely be achieved for severe traumatic brain injury patients. Above illustrate the tilt tabled device. Patient is started from a flat position (a), and undergoes verticalization and tilting (b and c).

CONCLUSION

Studies in general critical care patients suggest functional improvement with early mobilization (<72 h). However, the type, dose, intensity, and frequency of early mobilization remains poorly defined. The role of early mobilization is still being elucidated in neurocritical care as RCTs are lacking. While potential benefits have been identified, some patients, for example, those with AIS may have worse outcomes with VEM (<24 h). In stable neurocritical care disorders, progression from head of bed elevation to out of-bed and walking may have modest benefits. Ongoing studies of exercise physiology, virtual reality, and electrical muscle stimulation may help further determine the effect of early mobilization in the neurocritical care unit.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

■ of special interest
■■ of outstanding interest

1. Winkelman C. Inactivity and inflammation in the critically ill patient. Crit Care Clin 2007; 23:21–34.
2. Kho ME, Molloy AJ, Clarke FJ, *et al.* Multicentre pilot randomised clinical trial of ■ early in-bed cycle ergometry with ventilated patients. BMJ Open Respir Res 2019; 6:e000383.

The feasibility of early in-bed cycling in 66 mechanically ventilated patients was demonstrated in a pilot RCR.

3. Maffei P, Wiramus S, Bensoussan L, *et al.* Intensive early rehabilitation in the intensive care unit for liver transplant recipients: a randomized controlled trial. Arch Phys Med Rehabil 2017; 98:1518–1525.
4. McWilliams D, Jones C, Atkins G, *et al.* Earlier and enhanced rehabilitation of ■ mechanically ventilated patients in critical care: a feasibility randomised controlled trial. J Crit Care 2018; 44:407–412.

In this single center feasibility trail patients ventilated more than 5 days 103 patients were randomized to earlier rehabilitation or standard intervention. Patients in the intervention arm mobilized earlier and reached a higher level of mobility at the point of critical care discharge.

5. Sarfati C, Moore A, Pilorge C, *et al.* Efficacy of early passive tilting in minimizing ICU-acquired weakness: a randomized controlled trial. J Crit Care 2018; 46:37–43.
6. Denehy L, Lanphere J, Needham DM. Ten reasons why ICU patients should be mobilized early. Intensive Care Med 2017; 43:86–90.
7. Harper CM, Lyles YM. Physiology and complications of bed rest. J Am Geriatr Soc 1988; 36:1047–1054.
8. Fortney S, Schneider V, JE G. The physiology of bedrest. The handbooks of physiology. New York: Oxford University Press; 1996; 889–939.
9. Zhang L, Hu W, Cai Z, *et al.* Early mobilization of critically ill patients in the ■ intensive care unit: a systematic review and meta-analysis. PLoS One 2019; 14:e0223185.

The meta-analysis included 23 randomized controlled trials (RCTs) and 2308 patients. Early mobilization may reduce the incidence of ICU-acquired weakness, increase the proportion of standing patients, increase the number of ventilator free days, increase the distance of unassisted walking, and increase home discharge.

10. Puthucheary ZA, Rawal J, McPhail M, *et al.* Acute skeletal muscle wasting in critical illness. JAMA 2013; 310:1591–1600.
11. Baldwin MR, Reid MC, Westlake AA, *et al.* The feasibility of measuring frailty to predict disability and mortality in older medical intensive care unit survivors. J Crit Care 2014; 29:401–408.
12. Bahouth MN, Power MC, Zink EK, *et al.* Safety and feasibility of a neu- ■ roscience critical care program to mobilize patients with primary intracerebral hemorrhage. Arch Phys Med Rehabil 2018; 99:1220–1225.

Intracerebral hemorrhage patients were compared pre ($n=28$) and post ($n=29$) a mobility algorithm rollout. Patients in the postintervention group were significantly more likely to undergo mobilization within the first 7 days after admission without an increase in complications.

13. Swanson EW, Mascitelli J, Stiefel M, *et al.* Patient transport and brain oxygen in comatose patients. Neurosurgery 2010; 66:925–931; discussion 31–32.
14. Murphy TH, Corbett D. Plasticity during stroke recovery: from synapse to behaviour. Nat Rev Neurosci 2009; 10:861–872.
15. Schweickert WD, Pohlman MC, Pohlman AS, *et al.* Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009; 373:1874–1882.
16. Moss M, Nordon-Craft A, Malone D, *et al.* A randomized trial of an intensive physical therapy program for patients with acute respiratory failure. Am J Respir Crit Care Med 2016; 193:1101–1110.
17. Tipping CJ, Harrold M, Holland A, *et al.* The effects of active mobilisation and rehabilitation in ICU on mortality and function: a systematic review. Intensive Care Med 2017; 43:171–183.
18. Doiron KA, Hoffmann TC, Beller EM. Early intervention (mobilization or active ■■ exercise) for critically ill adults in the intensive care unit. Cochrane Database Syst Rev 2018; 3:CD010754.

Four RCTs with 690 patients of early mobilization in the ICU were examined. The evidence is low quality for methodological reasons and does not demonstarte a clear benefit to early mobilization in the ICU. However, additional trials are ongoing.

19. Schaller SJ, Anstey M, Blobner M, *et al.* Early, goal-directed mobilisation in the surgical intensive care unit: a randomised controlled trial. Lancet 2016; 388:1377–1388.
20. Schaller SJ, Scheffenbichler FT, Bose S, *et al.* Influence of the initial level of ■■ consciousness on early, goal-directed mobilization: a post hoc analysis. Intensive Care Med 2019; 45:201–210.

Post-hoc analysis of a RCT of 200 patients suggests that early (<72 h), goal-directed mobilization in patients with an impaired initial conscious state (Glasgow Coma Scale ≤8) is not harmful but effective.

21. Devlin JW, Skrobik Y, Gelinas C, *et al.* Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 2018; 46:e825–e873.
22. Wojner-Alexander AW, Garami Z, Chernyshev OY, Alexandrov AV. Heads down: flat positioning improves blood flow velocity in acute ischemic stroke. Neurology 2005; 64:1354–1357.
23. Olavarria VV, Arima H, Anderson CS, *et al.* Head position and cerebral blood flow velocity in acute ischemic stroke: a systematic review and meta-analysis. Cerebrovasc Dis 2014; 37:401–408.
24. Hargroves D, Tallis R, Pomeroy V, Bhalla A. The influence of positioning upon cerebral oxygenation after acute stroke: a pilot study. Age Ageing 2008; 37:581–585.
25. Mehagnoul-Schipper DJ, Vloet LC, Colier WN, *et al.* Cerebral oxygenation declines in healthy elderly patients in response to assuming the upright position. Stroke 2000; 31:1615–1620.
26. Titsworth WL, Hester J, Correia T, *et al.* The effect of increased mobility on morbidity in the neurointensive care unit. J Neurosurg 2012; 116: 1379–1388.
27. Hopkins RO, Spuhler VJ. Strategies for promoting early activity in critically ill mechanically ventilated patients. AACN Adv Crit Care 2009; 20:277–289.
28. Klein K, Mulkey M, Bena JF, Albert NM. Clinical and psychological effects of early mobilization in patients treated in a neurologic ICU: a comparative study. Crit Care Med 2015; 43:865–873.
29. Powers WJ, Rabinstein AA, Ackerson T, *et al.* Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019; 50:e344–e418.
30. French B, Thomas LH, Coupe J, *et al.* Repetitive task training for improving functional ability after stroke. Cochrane Database Syst Rev 2016; 11:CD006073.
31. Bernhardt J, Dewey H, Thrift A, *et al.* A Very Early Rehabilitation Trial for Stroke (AVERT): phase II safety and feasibility. Stroke 2008; 39:390–396.
32. AVERT Trial Collaboration Group. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. Lancet 2015; 386:46–55.
33. Karic T, Roe C, Nordenmark TH, *et al.* Impact of early mobilization and rehabilitation on global functional outcome one year after aneurysmal subarachnoid hemorrhage. J Rehabil Med 2016; 48:676–682.
34. Karic T, Roe C, Nordenmark TH, *et al.* Effect of early mobilization and rehabilitation on complications in aneurysmal subarachnoid hemorrhage. J Neurosurg 2017; 126:518–526.

35. Karic T, Sorteberg A, Haug Nordenmark T, *et al.* Early rehabilitation in patients with acute aneurysmal subarachnoid hemorrhage. Disabil Rehabil 2015; 37:1446–1454.
36. Olkowski BF, Shah SO. Early mobilization in the neuro-ICU: how far can we go? Neurocrit Care 2017; 27:141–150.
37. ■■ Young B, Moyer M, Pino W, *et al.* Safety and feasibility of early mobilization in patients with subarachnoid hemorrhage and external ventricular drain. Neurocrit Care 2019; 31:88–96.

The single-center feasibility trial demonstrated that nurse-driven mobilization for patients with external ventricular drains (EVDs) is safe, feasible, and can session increase the odds of discharge to home or in-patient rehabilitation.

38. ■■ Shah SO, Kraft J, Ankam N, *et al.* Early ambulation in patients with external ventricular drains: results of a quality improvement project. J Intensive Care Med 2018; 33:370–374.

In this single-center prospective, observational study in 90 patients demonstrated that early physical therapy is feasible and safely tolerated in patients with EVDs.

39. ■■ Yataco RA, Arnold SM, Brown SM, *et al.* Early progressive mobilization of patients with external ventricular drains: safety and feasibility. Neurocrit Care 2019; 30:414–420.

In this single-site, retrospective chart review of 153 patients with EVD, early mobilization was found to be feasible and safe.

40. Hemphill JC 3rd, Greenberg SM, Anderson CS, *et al.* Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2015; 46:2032–2060.
41. Liu N, Cadilhac DA, Andrew NE, *et al.* Randomized controlled trial of early rehabilitation after intracerebral hemorrhage stroke: difference in outcomes within 6 months of stroke. Stroke 2014; 45:3502–3507.
42. Cullen N, Meyer M, MacKenzie H, et al. Evidence Based Review of Moderate-Severe Acquired Brain Injury 12th edition. 2019. https://erabi.ca/resources/.
43. Andelic N, Bautz-Holter E, Ronning P, *et al.* Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic brain injury? J Neurotrauma 2012; 29:66–74.
44. Elliott L, Coleman M, Shiel A, *et al.* Effect of posture on levels of arousal and awareness in vegetative and minimally conscious state patients: a preliminary investigation. J Neurol Neurosurg Psychiatry 2005; 76:298–299.
45. Newman M, Barker K. The effect of supported standing in adults with upper motor neurone disorders: a systematic review. Clin Rehabil 2012; 26:1059–1077.
46. Chang AT, Boots RJ, Hodges PW, *et al.* Standing with the assistance of a tilt table improves minute ventilation in chronic critically ill patients. Arch Phys Med Rehabil 2004; 85:1972–1976.
47. ■ Riberholt CG, Lindschou J, Gluud C, *et al.* Early mobilisation by head-up tilt with stepping versus standard care after severe traumatic brain injury – protocol for a randomised clinical feasibility trial. Trials 2018; 19: 612.

The protocol for a trial is to assess the feasibility of an intensive physical rehabilitation intervention focusing on mobilization to the upright position in severe traumatic brain injury patients is described.

48. Medicine CfSC. Early acute management in adults with spinal cord injury: a clinical practice guideline for healthcare professionals. J Spinal Cord Med 2008; 31:403–479.
49. Herzer KR, Chen Y, Heinemann AW, Gonzalez-Fernandez M. Association between time to rehabilitation and outcomes after traumatic spinal cord injury. Arch Phys Med Rehabil 2016; 97:1620–1627.e4.