Mobilization of the Patient After Neurological Insult

Literature Review

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Introduction

Hospitalized patients are at high risk for immobilization as a result of acute illness, the presence of invasive lines and monitoring devices, and other safety concerns.[1] Immobilization and inactivity during hospitalization are associated with a multitude of musculoskeletal,[2-8] cardiovascular,[9-12] and hematologic[9,13] pathologies, along with persistent weakness and higher mortality rates.[14-16] Intensive care unit (ICU) patients can experience ICU-acquired weakness within 24 hours of ICU admission, leading to ongoing functional impairment that can necessitate years of treatment to achieve peak physical functional recovery.[17-19] Early progressive mobilization has been shown to be safe and feasible and has been associated with improved functional outcomes, better quality of life, reduced hospital costs, and decreased length of hospitalization among certain patient populations.[16,20-22] Though multiple professional organizations have endorsed the practice of early mobilization in specific patient populations,[23-25] practice guidelines to direct early mobilization in the care of the general neuroscience patient do not exist. Evidence-based recommendations are needed to guide nurses in safe and effective implementation of early mobilization practices in this patient population. For this reason, the American Association of Neuroscience Nurses (AANN) formed a writing group with the aim of conducting a systematic literature review to evaluate the evidence and determine best practice recommendations for early mobilization of neuroscience patients.

Methods

The AANN Clinical Practice Guideline (CPG) Board of Directors framed the scope of this review and drafted five questions formatted according to formatted according to the patient/population, intervention, comparison, and outcome (PICO) methodology.[26] The writing group was designated by the AANN CPG Board of Directors from a pool of candidates drawn from the response to a call for volunteers. With the assistance of a biomedical librarian, the writing group conducted a systematic literature search through the PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, and Cochrane Library databases using relevant Medical Subject Headings (MeSH) terms and keywords. Full search methodology is available in the Appendix. Inclusion criteria included full-text articles with adult sample populations (>17 years), written in English, and published in peer-reviewed journals. Nonexperimental observational studies and quality improvement (QI) publications were included in the review because of the overall scarcity of published research relevant to the predetermined PICO questions. The timeframe was established to include all relevant publications since 2000.

Search results revealed 741 articles (see the Appendix for a full PRISMA diagram, p. 11). One hundred eight duplicates were removed; 29 others were nonjournal articles or not available in English and therefore were removed. An additional 48 citations without abstracts were removed, resulting in an upload of 556 references to the systematic review software (DistillerSR, Evidence Partners, 2020).

The systematic literature review consisted of three levels of review: (1) title/abstract review, (2) full text review, and (3) risk of bias assessment. The Risk of Bias In Nonrandomized Studies–of Interventions (ROBINS-I) tool[27] and the Cochrane Risk of Bias tool[28] were used to assess bias in nonrandomized (including QI articles) and randomized studies, respectively. At each step, two reviewers (MS, MM, BY, JC) independently reviewed each article. Conflicts between reviewers at any step were discussed until consensus was achieved before the group proceeded to the next step. If needed, a third reviewer was consulted as a tiebreaker. As a final step, articles were assigned to the appropriate PICO question. Articles assigned to each PICO question were summarized in evidence tables (see the Appendix, pp. 12–26) and critically evaluated. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology[29] guided the determination of quality of evidence and recommendation statements, which were reviewed and approved by all members of the writing group. Internal and external reviewers subsequently reviewed the resulting manuscript of recommendations before final approval by the AANN CPG Board of Directors.

Results

The following information is organized by PICO question, with synthesis of relevant literature and a recommendation statement to accompany each question.

1. Timing of Mobilization and Mortality and Functional Recovery After Ischemic Stroke

What is the impact of timing of mobilization on mortality and functional recovery among patients with acute ischemic stroke?

Recommendation: Among patients with acute ischemic stroke, we recommend against out-of-bed mobilization within 24 hours of stroke onset but are in favor of out-of-bed mobilization beginning within 24 to 48 hours after stroke. (Moderate Recommendation, Moderate Level of Evidence)

Rationale: Fifteen articles (n = 3,588 unique patients) matched the focus of this PICO question.[30-44] Of these, five studies were limited exclusively to patients with ischemic stroke.[34,36,37,41,43] The remaining 10 studies included a sample population comprising multiple types of strokes.[30-33,35,38-40,42,44] Individual study characteristics are available in the Appendix.

The timing of mobilization after ischemic stroke is variable and often is categorized as very early mobilization (VEM), early mobilization (EM), or late/delayed mobilization. VEM commonly refers to out-of-bed activity within the first 24 hours after stroke, EM refers to out-of-bed activity within 24 to 48 hours after stroke, and activity commencing more than 48 hours after stroke often is categorized as late/delayed mobilization.[31,33,34,39,40,42,43]

Mortality

Six articles in this review reported mortality outcomes.[38-40,42-44] One study (n = 227) assessed between-group mortality differences at hospital discharge and found no statistical difference between a VEM, EM, and late mobilization group.[40] The remaining five studies (range, n = 37–2,104), two of which were pilot studies,[38,43] all compared a VEM or EM protocol to usual care and found no differences in mortality at 3 months after stroke.[38,39,42-44] One limitation of the findings from each of these six articles is use of a weakly defined usual care group as the control or comparison group. This limitation introduces the possibility of dynamic control conditions over the course of the study and possible compensatory equalization of treatment between the control and intervention groups. Despite these limitations, there is promising evidence that although VEM and EM have not been found to decrease mortality at hospital discharge or 3 months after stroke, the odds of mortality at these time points also are not greater in patients who are mobilized.

Functional Recovery

Determination of the impact of mobilization on functional recovery in this review is based on follow-up assessments typically conducted at 3 to 12 months after hospital discharge.[30-35,37-39,41-44] Conceptualization of functional recovery is variable (e.g., independence in activities of daily living, severity of disability symptoms, balance recovery, exercise capacity, muscle strength, return to work). The articles in this review primarily dichotomize functional recovery as either poor or good, using Modified Rankin Scale (mRS) scores 0 through 2 as indicators of good recovery. It is important to note that significant heterogeneity of measurement selection across studies makes the synthesis of findings a challenge.

In the past decade, an increasing number of randomized controlled trials (RCTs) have examined the impact of VEM or EM on functional recovery among patients with both ischemic and hemorrhagic stroke.[31-39,41,43,44] Three major factors limit evaluation of these studies: (1) low patient enrollment and therefore statistical underpowering of individual study findings, (2) difficulty disentangling the effects of mobilization timing and mobilization dose/intensity, and (3) variability in mobilization intervention methods among studies.

The most robust study evaluating functional outcomes related to the timing of early mobilization after acute ischemic stroke is the Phase III AVERT (A Very Early Rehabilitation Trial) trial.[39] This international, multicenter RCT, which analyzed more than 2,000 patients' data, compared the impact of VEM versus only usual stroke care on mRS score and time to walking 50 meters, among other variables.[39] In this study, participants randomized to VEM had less favorable outcomes, defined by mRS score, than those randomized to usual care. Secondary outcomes did not differ between groups. Findings from AVERT caution against mobilization within the first 24 hours after stroke, although it is important to note that there were limitations to control standards in the usual care group Throughout the study period, the time to first mobilization decreased in the usual care group so that two-thirds of the usual care group received out-of-bed activity within 24 hours of stroke onset (median, 22.4 hours). Also of note, the VEM intervention in this trial was implemented as an addition to usual care standards. Therefore, the daily and total amount and frequency of mobilization differed

significantly between the VEM and usual care groups (p<.0001), in combination with differences in the timing of first mobilization. Similar trends also were noted in several smaller studies, although not all findings reached statistical significance.[33,34,37]

In contrast, several studies reported more favorable functional outcomes in association with VEM compared with standard care or delayed mobilization.[31,35,40,42] In light of these findings, it is reasonable to exercise caution in promoting intensive, out-of-bed mobilization within the first 24 hours after stroke; however, there may be benefits to initiating mobilization between 24 and 48 hours after stroke. Further research is needed to determine the best mobilization methods and dose (e.g., frequency, intensity, time, and type) for optimizing early functional recovery after acute ischemic stroke.

2. Hospital and Functional Outcomes in Critically Ill Patients

Among critically ill patients with neurological insult, what is the impact of EM, compared to standard-of-care mobilization, on hospital (mortality, length of stay) and functional outcomes (Functional Independent Measure [FIM]/mRS score at discharge and 6 to 12 months)?

Recommendation: Among critically ill patients with neurological insult, there is insufficient high-quality evidence to support EM as a mechanism to decrease mortality, reduce hospital or ICU length of stay, or improve functional outcomes. However, in the absence of reports of negative outcomes associated with EM, we recommend mobilization of critically ill patients with neurological insult as hospital and unit-based resources safely allow. (Good Practice Recommendation)

We strongly urge ongoing research to determine the efficacy of EM in specific subpopulations of neurocritically ill patients.

Rationale: Fifteen articles (n = 4,821 unique patients) matched the aims of this PICO question. The earliest publication included in this review was from 2002, with nearly all of the remaining publications representing work conducted since 2015, thus indicating that EM research in the neurocritical care population is a novel and still-evolving area of interest. The median sample size was 124 (range, 45–2,645). The reviewed studies represent heterogeneous sample populations, where a number of studies were inclusive of all patients admitted to the ICU (i.e., ischemic and hemorrhagic stroke, status epilepticus, cerebrovascular malformations, neuromuscular disorders, central nervous system infections, brain tumors, and head and spine trauma).[45-50] Across all studies, the most commonly studied population was aneurysmal subarachnoid hemorrhage.[51-56] One study observed acute stroke patients,[40] one specifically studied patients with intracerebral hemorrhage,[57] and three included only patients with an external ventricular drain.[51,56,58]

Of the 15 included articles, the majority were prospective observational studies (n = 7 studies).[40,45,49,51,53,54,56] Only one study was a randomized experiment,[50] three used quasi-experimental design,[48,55,57] and the remaining studies were retrospective chart reviews.[46,47,52,58] The lack of randomized experiments among neurocritically ill patients represents a significant opportunity for future research to strengthen relational inferences related to the impact of EM in this patient population.

The majority of studies (n = 12) included reports of one or more in-hospital clinical outcome (e.g., mortality and length of stay).[40,45-49,51,52,55-58] Only five studies specifically reported mortality outcomes, with mixed findings.[40,48,55,57,58] Mulkey et al.[48] reported decreased 30-day mortality in a higher mobility group (p<.001), and Yataco et al.[58] reported 83% survival rate at hospital discharge in a retrospective cohort review, although without a comparison group. In contrast, three studies reported no differences in mortality rates between an EM group and a comparison group.[40,55,57] No studies reported associations between EM and increased mortality during the acute or postacute recovery phase.

Findings related to both hospital and ICU length of stay were similarly conflicting. Hester et al.[46] and Klein et al.[45] both reported statistically significant reductions in hospital (p<.001 for both) and ICU (p = .031 and p = .001, respectively) length of stay following implementation of an EM program in an adult neuro ICU population. Olkowski et al.[52] and Mulkey et al.[48] also reported earlier hospital discharge (p = .013 and p<.001, respectively) in earlier or higher mobilization groups when compared with historical data or groups undergoing lower levels of mobilization. Although no studies reported associations between EM and longer hospitalization, several studies have reported no benefit in length of stay metrics with implementation of an EM intervention.[47,51,55,56] Bartolo et al.[49] reported increased ICU length of stay in an EM group compared with standard care; however, the study's observational design inhibits the ability to determine causation. Overall, the synthesis and generalizability of these findings is extremely limited by variation in study design and sample population, small sample size, and the overall paucity of studies. Further rigorous experimental research is needed to determine the impact of EM on hospital and ICU length of stay, as well as additional quality measures, among specific critical neurological conditions.

The efficacy of EM in the neuro ICU to improve physical function at hospital discharge and across time remains

unclear. Findings of this review support the hypothesis that EM in neurocritically ill patients is associated with improved physical function at the time of hospital discharge compared with standard care.[40,49,53,54] However, the certainty of this conclusion is far from definitive. Though several studies reported improved FIM[40,53] or other mobility scale scores[49,54] from the time of hospital admission to hospital discharge among patients who underwent EM, the interpretation of these findings remains limited by nonexperimental design, the lack of a comparison group,[53] and limited consideration of important, potentially confounding variables in statistical analyses. Of note, the RCT in this review found no difference between groups in functional independence at hospital discharge ($p = 0.53$).[50] Though the efficacy of EM to improve functional independence among neurocritically ill patients remains largely indeterminate, no studies in this review reported worse functional outcomes as a result of EM. No studies in this review examined associations of EM with functional outcomes beyond hospital discharge, revealing limitations in our understanding of how EM impacts long-term clinical outcomes in this population.

This review brings to light several important research opportunities. First, there is a need for high-quality randomized experiments to examine the impact and efficacy of EM in various neurological diagnoses encountered in the ICU. Outcomes of interest include associations of EM with in-hospital outcomes, including mortality, gains in functional independence, muscle strength, duration of mechanical ventilation, ICU and hospital length of stay, and delirium. It is also important to further expand future research to determine the impact of EM in neurocritically ill patients on long-term multidimensional outcomes, such as cognitive recovery and psychiatric morbidities. Furthermore, the ideal modalities, dose, timing, and duration of mobilization and exercise for optimizing outcomes in critically ill neuroscience patients remain indeterminate.

3. Patient Safety Events

Among critically ill patients with neurological insult, what is the impact of EM on patient safety events?

Recommendation: Although there are limited randomized trials that examine patient safety events as a primary endpoint, there is moderate-to-low quality evidence to support the safety of EM beginning within 24 to 72 hours after hospital admission in critically ill patients with neurological insult. (Moderate Recommendation, Low Quality of Evidence)

This recommendation is limited by inability to specify an optimal modality, intensity, or dosage of mobilization and to address safety events that may not have been measured in the reviewed studies. Safety events related to the timing of specific EM efforts and the intensity and type of EM should be evaluated in multicenter experimental trials.

Rationale: Patient safety events were defined by the writing group *a priori* as device dislodgement (including external ventriculostomy), falls, nosocomial infections, venous thromboembolism, and pressure injury. Although they do not represent an exhaustive list of all possible safety measures, the selected measures align with the Agency for Healthcare Research and Quality Patient Safety Indicators,[59] the National Quality Forum's nursing performance indicators,[60] and American Nurses Association's nursing-sensitive quality indicators.[61]

Twenty-two articles (n = 5,178 unique patients) met the focus of this PICO question,[20,33,34,38,42,45-47,49,51,52,55-58,62-68] the majority of which were observational studies (see the Appendix). Few to no adverse events have been associated with EM among critically ill patients with neurological insults.[20,38,42,49,51,52,55-58,62,63,66,67] Few transient adverse events, such as headache, nausea, blood pressure changes, lethargy, increases in intracranial pressure, and drain malfunction, have been reported in association with EM.[56,58] It is possible that defining premobilization screening criteria may have helped prevent more serious adverse events in critically ill patients.[56] In light of these findings, it is important to note that the mobilization methods in this review were highly heterogeneous and not well controlled in terms of measuring and controlling for the dose, intensity, and timing of mobilization. Also, several studies used a customized mobilization pathway that was not replicated in other studies.[20,45,51,55-57,63] Physiotherapists performed the mobilization strategies in the majority of the studies included in the review. Nine studies included nurse participation in the mobilization activity.[20,33,38,42,45,46,51,57,63] It is important to consider the personnel required to accomplish safe EM in the neuro ICU and to acknowledge that physiotherapy resources reflected in research protocols may outnumber those routinely available in everyday clinical practice.

Early Mobilization with External Ventriculostomy Drainage Catheter

Four observational studies reported no external ventriculostomy drainage (EVD) catheter dislodgment attributable to EM.[46,51,56,57] Use of a mobilization protocol with integrated formal catheter securement safety checks has been reported as adequate to prevent unintended catheter dislodgement[56,62] and cerebrospinal fluid leakage.[56]

Early Mobilization and Falls

Four studies assessed falls as an adverse event related to EM.[42,46,57] One large RCT comparing a VEM protocol (within 24 hours after stroke) to usual care reported no significant differences in fall rates between groups.[42] In a retrospective cohort analysis, the rates of falls and falls with injuries were similar before and immediately after implementing a Progressive Upright Mobility Protocol (PUMP) Plus program.[46] Patients who received out-of-bed mobilization in the first 72 hours after stroke experienced fall rates similar to those of patients who remained on bed rest (3.3% vs. 1.9%, respectively; $p = .47$).[68] Finally, no falls were associated with a progressive mobility program used on patients with intracerebral hemorrhage admitted to a neurocritical critical care unit.[57]

Early Mobilization and Nosocomial Infections

Preliminary data on this topic suggest a neutral-to-decreased incidence of hospital-acquired infections with the implementation of an EM protocol in critically ill patients with neurological insults. Implementation of the PUMP Plus program has been associated with reduced rates of hospital-acquired infections ($p<.05$) and ventilator-associated pneumonia ($p<.001$). A retrospective analysis of clinical outcome data before, immediately following, and 2 years after implementation of the PUMP Plus program reported a 50% reduction in hospital-acquired infections over the 2-year study period.[46] Naito et al. also reported significantly lower pneumonia rates in stroke patients who were out of bed in the first 72 hours after stroke compared with those who remained on bed rest (45.5% vs. 62.5%; $p<.01$).[68] No difference was noted between groups in the proportion of patients who developed a urinary tract infection (mobilized group = 8.3%, bed rest = 11.5%; $p = .31$).[68] No studies reported increased rates of hospital-acquired infections in association with EM.

Early Mobilization and Venous Thromboembolic Events

The incidence of deep vein thrombosis (DVT) and pulmonary emboli (PE) was significantly lower in an EM cohort compared with a historical comparison group (7.5% vs. 21%, respectively; $p = .0004$).[63] Diserens et al.[34] conducted a pilot RCT trialing early versus delayed out-of-bed mobilization for patients with acute ischemic stroke. Primary outcomes demonstrated no increase in total complications with an EM protocol after acute ischemic stroke. The incidence of severe complications, including PE, was greater in the group with prolonged best rest (47% vs. 8% in the EM group).[34]

Early Mobilization and Pressure Injury

The direct impact of EM on the development of new pressure injuries in critically ill patients with neurological insult is inconclusive. However, there is little evidence that EM worsens pressure injury rates. In one study, the mobilized patient group had significantly more acquired pressure injuries than the control group (27.1% vs. 9.4%, respectively; $p = .047$).[49] The interpretation of these findings warrants caution, however, because there were baseline demographic differences between the study groups, revealing that the control group had a more severe clinical and functional profile than the mobilized patient group.[49] In fact, Klein et al.[45] report that compared with a preintervention cohort, postintervention patients who participated in an EM protocol had fewer hospital-acquired pressure injuries (preintervention, 3.8% vs. postintervention, 1.1%; $p = .026$). The remaining studies showed no significant differences in pressure injury rates between those who were mobilized early and those who were treated as a standard care or control group.[20,68]

There are several limitations for this literature review. The majority of the studies included in this review represent small, single-center designs. Of the 22 articles included in the review, just two were non-pilot RCTs. Fifteen studies were considered low-quality research because of their prospective observational or retrospective designs. For the most part, these studies were not statistically powered to detect safety outcomes. In addition, the majority of the studies included a homogeneous patient population that limited the generalizability of the findings to a real-world, heterogeneous neuroscience patient population.

4. Safety and Functional Outcomes in the Acute Rehabilitation Setting

Among patients with neurological impairment in the acute rehabilitation setting, what is the effect of mobilization on safety events and functional outcome (at rehab discharge and 6 to 12 months)?

Recommendation: There is insufficient evidence to support a practice recommendation that impacts specific safety events for mobilization of patients with neurological impairment in an acute inpatient rehabilitation setting. (Good Practice Statement)

There is insufficient evidence to support a practice recommendation that impacts functional outcomes 6 to 12 months after discharge from an acute inpatient rehabilitation setting. Though there is no single mobilization approach in the acute inpatient rehabilitation setting that is known to improve long-term functional outcomes,

existing theory-driven rehabilitation approaches appear to offer some benefit to functional recovery after stroke. (Good Practice Statement)

High-quality studies are needed to investigate the long-term efficacy of specific rehabilitation approaches in various neuroscience populations.

Rationale: There is limited literature evaluating the effect of mobilization on safety events and functional outcomes for patients with neurological impairment in the acute rehabilitation setting. Five studies were found suitable to address this question.[30,69-71] All studies were of low-to-moderate strength, given their small sample sizes and the prevalence of missing data.

Functional Outcomes

Overall, mobilization of neurologically impaired patients in the acute rehabilitation setting has been found to be safe, with no adverse events reported in the literature. Characteristics of those reported to benefit from early mobilization, as measured by improved mRS and Barthel Index scores at 6 months after neurological insult, include younger patients with adequate bowel and bladder control and without Total Anterior Circulation Infarct syndrome.[30] Tilt table exercises in the acute rehabilitation setting may help improve quality of life and muscle strength in patients who experience hemiplegia after a stroke.[71] Yadav et al. reported significant improvement in absolute lower limb function, elbow flexion, and knee extension with 1 month of robotic tilt table exercises after stroke.[71] Of note, a conventional tilt table promoted improvement in level of consciousness compared to a tilt table with stepping, although not significantly more than conventional tilt table therapy alone (Coma Recovery Scale–Revised median increase of 5 vs. 2, respectively).[69] Importantly, the studies in this review primarily examine very specific types of therapeutic exercises. As such, functional outcome findings cannot necessarily be generalized to all types of mobilization exercises or to all neuroscience subpopulations.

There is weak evidence to suggest that early sitting, standing, and walking using a contemporary Bobath approach (CBA) may improve Berg Balance Scale scores 4 to 8 weeks after therapy.[70] In addition, in patients with severe motor deficits after stroke, Tang et al.[70] demonstrated significantly better lower extremity, basic mobility, and overall Stroke Rehabilitation Assessment of Movement scores after 4 and 8 weeks of therapy, albeit in a small sample size (n = 48). Finally, the use of mirror therapy was shown to improve Fugl-Meyer Assessment extremity subscale scores and Brunel Balance Assessment scores in patients who have had an acute stroke.[72]

Safety Events

The reviewed studies did not report any adverse safety events, although one study reported more frequent interruptions to therapy with the use of a tilt table plus stepping device versus conventional tilt table therapy alone.[69]

5. Timing of Mobilization After Intravenous Thrombolysis and Hospital Outcomes and Safety Events

Among patients with acute ischemic stroke who receive intravenous (IV) thrombolysis, what is the impact of EM (less than 24 hours after drug administration) compared to delayed ambulation (more than 24 hours after drug administration) on patient's hospital outcomes and safety events?

Recommendation: There is insufficient evidence to support a practice recommendation for EM, as it relates to impact on in-hospital outcomes and safety events, in the ischemic stroke patient population who receives IV thrombolysis. There is a need for further scientific research exploring clinical outcomes related to EM in the population of patients who have had acute ischemic stroke and received IV thrombolysis versus mechanical thrombectomy, specifically. (Good Practice Statement)

Rationale: There is limited high-quality research to support EM practices in the population of patients who have had an acute ischemic stroke and received IV thrombolysis. The majority of studies examining EM in acute stroke populations included both ischemic and hemorrhagic stroke patient populations.[33,38-40,42,44,73,74] Only three studies included in this review assessed the impact of EM specifically in an ischemic stroke population that received IV thrombolysis.[41,43,75]

The benefits of early sitting in the ischemic stroke patient population were evaluated in the Early Sitting in Ischemic Stroke Patients (SEVEL) multicenter RCT.[41] Patients in the randomized group were seated out of bed at the earliest possible time, but no later than one calendar day after stroke onset. The progressive sitting group was seated out of bed on the third calendar day after stroke onset. The primary outcome was mRS score at 3 months after stroke. Secondary outcomes included the prevalence of medical complications, length of hospitalization, and sitting tolerance. The analysis and generalizability of findings were limited by low recruitment and follow-up rates. Data were analyzed from 138 patients, 63 in the early sitting group and 75 in the progressively sitting group. There were no significant differences in primary or secondary outcomes between the early-sitting and progressive-sitting study groups. Primary outcome was assessed 3 months after stroke; the

secondary outcomes were assessed at 7 days or 3 months post-stroke. Fatigue was assessed only at the 3-month follow-up. The amount of time a patient was positioned out of a bed in a chair was documented.[41]

The second study, a randomized single-blind controlled pilot trial, evaluated the safety, feasibility, and benefit of EM compared to routine physical therapy in patients who have had an acute ischemic stroke.[43] Primary study outcomes included in-hospital mortality and morbidity. Secondary outcomes included functional status at 14 days and 3 months post-stroke, as measured by the National Institutes of Health Stroke Scale (NIHSS) and mRS scores. The mobilization intervention focused on sitting out of bed in a chair or standing (whenever and as soon as possible) and conducting functional training and motor relearning. Thirty-three percent of patients in the intervention group received thrombolytic treatment, and 37% of patients in the control group received thrombolytic treatment. The median time from stroke symptom onset to first mobilization was 43 hours in the intervention group versus 72 hours in the control group. Although this study is limited by a small sample size (n = 37), EM after acute ischemic stroke was found to be safe and feasible. No statistically significant differences were observed between groups on the primary or secondary outcomes. There was no statistical difference between groups when functional independence, disability, or activities of daily living were assessed at the 3-month follow-up.[43]

Most recently, Silver et al. compared discharge outcomes and several safety events among patients with ≥12 hours of bed rest versus ≥24 hours of bed rest after stroke thrombolysis.[75] The group that was mobilized earlier had shorter average hospital stay (3.5 vs. 5.4 days; $p = .006$). This same group also experienced a lower incidence of pneumonia (1.6% vs. 8.3%; $p = .006$). However, the proportion of patients with a favorable discharge disposition did not significantly differ between groups (adjusted OR, 1.20; 95% CI, 0.71–2.03; $p = .50$).[75]

All of the studies reviewed were low-quality evidence. Since publication of these studies, mechanical thrombectomy has emerged as an additional mainstay of treatment for acute ischemic stroke. Research examining the impact that the timing, method, dose, and frequency of EM has on in-hospital clinical outcomes and safety events in the acute ischemic stroke patient population who receive IV thrombolysis and/or mechanical thrombectomy is needed.

Summary

This AANN review of the literature on mobilization of the patient after neurological insult was intended to provide a summary of evidence and best practice guidance for specific PICO questions germane to mobilization of the neuroscience patient. Overall, there is a need for more high-quality research before strong practice recommendations can be made. Although the evidence to support the recommendations in this document is largely preliminary, it is sufficient to support EM in the neuroscience population as a safe, if not efficacious, practice. Even among neurocritically ill patients in the ICU, mobilization can be achieved without precipitating adverse safety events or worsening clinical outcomes. The precise mobilization modality, dose, and timing after acute neurological injury to optimize in-hospital and long-term functional outcomes remain unknown.

This literature review is limited to the scope of the predetermined PICO questions listed in this document. Therefore, it is not intended as a comprehensive review and does not fully address mobilization practices for all specific subsets of neuroscience patients. As reflected in the volume of available published literature, the preponderance of studies represents the acute stroke population. The recommendations contained in this CPG are limited to the adult neuroscience population and therefore may differ from recommended best practices for a pediatric population.

Appendix

Literature Search Strategy

PubMed Search

("neurology"[MeSH Terms] OR "neurology"[All Fields] OR "neurosurgery"[All Fields] OR "neuroscience nursing"[MeSH Terms] OR ("neuroscience"[All Fields] AND "nursing"[All Fields]) OR "neuroscience nursing"[All Fields] OR ("neurological"[All Fields] AND "nursing"[All Fields]) OR "neurological nursing"[All Fields] OR "neuroscience nursing"[tiab] OR "Critical Care"[Mesh] OR "Critical care nursing" OR "Critical care"[tiab] OR "acute care"[tiab] OR "neurointensive" OR "neuro ICU" OR "neurocritical" OR "neuro critical"[tiab] OR "stroke unit"[tiab] OR "acute stroke"[tiab] OR ((stroke[MH] OR "brain injuries"[MH]) AND (acute OR critical OR postoperative)) OR (("intracranial" OR "subarachnoid" OR "cerebral" OR cerebrovascular) AND (hemorrhage* OR bleed*)) OR "cerebrovascular trauma"[Mesh] OR "Brain Ischemia"[mesh] OR "brain injuries"[Mesh] OR AVERT[ti] OR AMOBES[tiab] OR SEVEL[tiab] OR "stroke rehabilitation"[Mesh]) AND ((mobili*[All Fields] AND (early[All Fields] OR timing[All Fields]) OR "early mobility"[tiab] OR "early ambulation"[Mesh] OR (mobiliz* AND "Time Factors"[Mesh]) OR "early physical activity"[tiab] OR "Progressive mobility"[tiab]))))) AND (((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomized[tiab] OR randomised[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh]))

CINAHL Search

((AB mobili* AND (early OR timing)) OR AB "early mobility" OR TI "early mobility" OR AB "early mobilization" OR AB "early mobilisation" OR TI "early mobilization" OR MH "Early Ambulation" OR AB "early ambulation" OR (mobiliz* AND MH "Time Factors") OR AB "early physical activity" OR AB "progressive mobility" OR TI "progressive mobility") AND (AB "acute stroke" OR TI "acute stroke" OR (MH "stroke" AND (Early OR Acute OR critical)) OR MH "Neuroscience Nursing+" OR "neuroscience nursing" OR AB "neurological nursing" OR "neurointensive" OR "neuro ICU" OR "neuroacute" OR "neurocritical" OR "neuro critical" OR AB "neurosurgery" OR (AB "neuroscience" AND "nursing") OR ((MH "Critical Care Nursing+" OR "Critical care nursing" OR "Critical care" OR "acute care") AND neurosurg*) OR (("intracranial" OR "subarachnoid" OR "cerebral" OR cerebrovascular) AND (hemorrhage* OR bleed*)) OR "cerebrovascular trauma" OR MH "Cerebral Ischemia" OR MH "brain injuries" OR TI "AVERT" OR TI "AMOBES" OR TI "SEVEL")

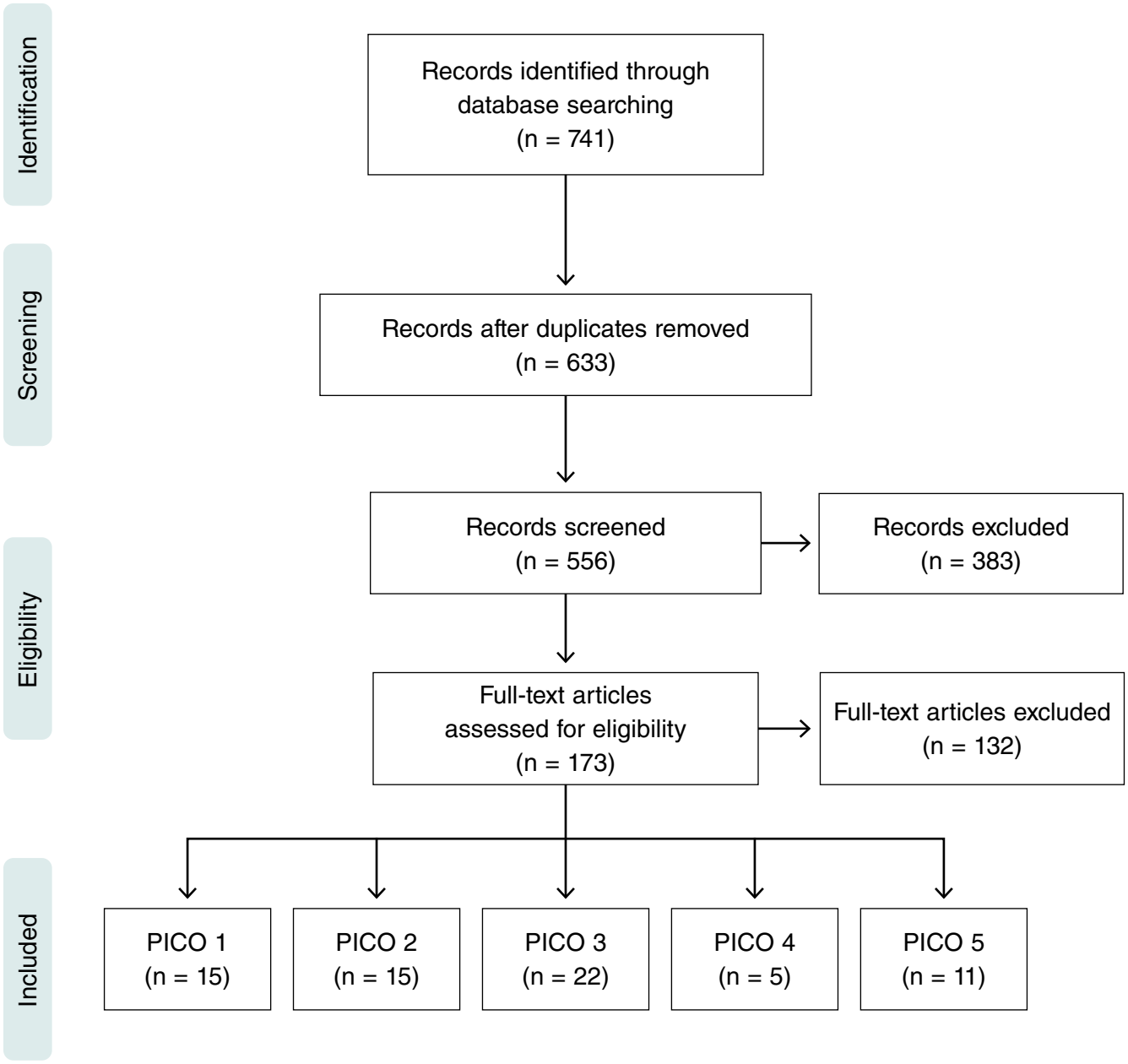
Embase Search

(('mobilization'/exp OR 'mobilization') AND (early OR 'timing'/exp OR timing) OR 'early ambulation':ti,ab OR 'early mobilisation':ti,ab OR 'early mobilization':ti,ab OR 'early mobility':ti,ab OR (mobiliz* AND ('time factor'/exp OR 'time factor')) OR 'early physical activity':ti,ab OR 'progressive mobility':ti,ab) AND (('cerebrovascular accident'/exp OR 'brain injury'/exp OR 'brain injury':ti,ab) AND (acute OR critical OR postoperative) OR 'acute stroke':ti,ab OR 'neurology'/exp OR 'neurology' OR 'neurology':ti,ab OR 'neurosurgery'/exp OR 'neurosurgery' OR 'neuroscience nursing'/exp OR 'neuroscience nursing' OR ((neurosurg* OR neurolog*) AND ('nursing'/exp OR nursing)) OR 'neurological nursing':ti,ab OR 'neurological intensive care unit'/exp OR 'neurological intensive care unit' OR 'neurointensive':ti,ab OR 'neuro icu':ti,ab OR (('intensive care'/exp OR 'intensive care' OR 'intensive care unit'/exp OR 'intensive care unit' OR 'intensive care nursing'/exp OR 'intensive care nursing' OR 'critical care':ti,ab) AND neurosurg*:ti,ab) OR 'cerbrovascular trauma' OR (cerbrovascular AND ('trauma'/exp OR trauma)) OR 'subarachnoid hemorrhage'/exp OR 'subarachnoid hemorrhage' OR 'brain ischemia'/exp OR 'brain ischemia' OR 'brain injury'/exp OR 'brain injury') AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) AND ('article'/it OR 'article in press'/it) AND [english]/lim

Cochrane Library Search

("early mobilization" OR "early mobility" OR "early ambulation" OR "early physical activity" OR "progressive mobility" OR ((early OR timing) AND (mobili*OR activity))) AND Stroke

PRISMA Diagram



Summary of Evidence

PICO 1. Timing of Mobilization and Mortality and Functional Recovery After Ischemic Stroke

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
AVERT Trial Collaboration Group, 2015	2,104	RCT	Ischemic stroke/ intracerebral brain hemorrhage (ICH)	To compare the effectiveness of frequent, higher-dose VEM (beginning within 24 hours of stroke onset) with usual care after stroke	Odds of favorable outcome (mRS 0–2) were lower in the VEM group (adjusted OR, 0.73; 95% CI, 0.59–0.90; p = .004)	High
Langhorne, 2017	2,104	RCT	Ischemic stroke/ICH	To compare VEM commencing within 24 hours of stroke to usual stroke unit care on mRS score, time to walking 50 meters, and serious adverse events at 3 months and quality of life at 12 months after stroke	Fewer patients in the VEM group had a favorable outcome at 3-month follow-up compared to the usual care group (adjusted OR, 0.73; 95% CI, 0.59–0.90; p = .004). Subgroup analyses tended to favor usual care, with the poorest outcomes in the VEM group with ICH, although no findings reached statistical significance (p>.05).	High
Bernhardt, 2008	71	RCT	Ischemic stroke/ICH	To compare mortality and functional outcomes between a VEM and usual care group at 3 months after stroke	More patients in the VEM group had a good outcome at 3 months (adjusted OR, 4.10; 95% CI, 0.99–16.88; p = .05), 6 months (adjusted OR, 4.17; 95% CI, 0.87–20.07; p = .08), and 12 months (adjusted OR, 8.15; 95% CI, 1.61–41.21; p = .01). More patients in the VEM group died (8 vs. 33; absolute risk difference = 12%; 95% CI, -4.3% to 28.2%; p = .20).	Moderate
Cumming, 2011	71	RCT	All stroke	To test the hypothesis that early (within 24 hours of stroke onset) and more intensive out-of-bed activity after stroke reduces the time to unassisted walking and improves independence in activities of daily living	Patients in the VEM group returned to walking 50 meters significantly faster than those in the control group (median, 3.5 vs. 7.0 days; p = .032). VEM was independently associated with better functional outcomes at 3 and 12 months.	Moderate
Herisson, 2016	138	RCT	Ischemic stroke	To evaluate the effect of early sitting (first 24 hours) versus progressive sitting (over first 3 days) on mRS scores at 3 months poststroke	There was no statistically significant difference in the proportion of favorable mRS scores (0–2) at 3 months between the two groups (early sitting, 76% vs. progressive sitting, 77%; p = 0.52).	Moderate
Langhorne, 2010	64	Pilot RCT	Ischemic stroke/ICH	To compare conventional stroke unit procedures with a progressive, nurse-led early mobility protocol and/ or automated physiological monitoring on mRS scores at 3 months after stroke	There was no statistically significant difference between the intervention and control groups in functional outcomes at 3 months (OR, 2.3; 95% CI, 0.3–18.0; p = .44).	Moderate

PICO 1. Timing of Mobilization and Mortality and Functional Recovery After Ischemic Stroke *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Kinoshita, 2017	227	Prospective observational	Ischemic/ hemorrhagic stroke	To compare the utility of the physiatrist and registered therapist operating acute rehabilitation (PROr) applied within 24 hours (very early), 24–48 hours (early), and ≥48 hours (late) after acute stroke on in-hospital mortality and changes in Glasgow Coma Scale (GCS), NIHSS, and FIM scores at hospital discharge	GCS scores at hospital discharge were significantly higher in the VEM group than in the EM or late groups (p<.05), but the gain of GCS did not significantly differ among the three groups (VEM: 0.9±0.2; EM: 0.7±0.2; late: 1.2±0.2; p>.05). Gains in total FIM and motor subscale scores were significantly greater in the VEM group compared with the other two groups (Total FIM: VEM: 32.6±3.0, EM: 20.2±2.3, late: 19.9±2.2; p<.001; Motor subscale: VEM: 28.5±2.7, EM: 17.7±2.1, late: 15.9±1.8; p<.001). There were no significant differences among the three groups in mortality (VEM: 4.3%, EM: 5.2%, late: 6.8%; p>.05).	Moderate
Franceschini, 2018	352	Longitudinal	All stroke	To assess early poststroke prognostic factors in patients admitted for postacute phase rehabilitation	EM initiated within 48 hours after stroke was significantly associated with favorable mRS scores (0–2) at 6 months compared with those mobilized more than 48 hours after acute stroke (OR, 2.31; 95% CI, 1.13–4.72; p = .022).	Moderate
Rahayu, 2019	40	RCT	Ischemic stroke	To compare the effect of EM started at 24 hours and 48 hours after ischemic stroke on balance and functional ability at days 5 and 7	The group mobilized at 24 hours had significantly higher Barthel Index scores on day 5 (55.05±11.15 vs. 38.94±13.47; p = .002) and day 7 than the group mobilized at 48 hours (70.90±17.93 vs. 56.45±20.79; p = .021).	Moderate
Diserens, 2012	42	Pilot RCT	Ischemic stroke	To evaluate the effect of early out-of-bed mobilization (hour 52) versus delayed out-of-bed mobilization (day 7) on the incidence of medical complications and differences in NIHSS and mRS scores	The proportion of participants with favorable mRS score at 3 months was similar between the EM group and delayed mobilization group (40% vs. 35%; p>.05).	Low
Sundseth, 2012	56	RCT	Ischemic stroke/ICH	To test the hypothesis that VEM within 24 hours after hospital admission improves outcome at 3 months poststroke compared with mobilization between 24 and 48 hours	Patients in the VEM group had nonsignificant higher odds of poor outcomes (adjusted OR, 2.70; 95% CI, 0.78–9.34; p = .73), mortality (OR, 5.26; 95% CI, 0.84–32.88; p = .08), and dependency (OR, 1.25; 95% CI, 0.36–4.34; p = .73).	Low
Sundseth, 2014	52	RCT	All stroke	To compare mRS scores at 3 months poststroke between patients mobilized within 24 hours versus within 24–48 hours of hospitalization	The timing of mobilization was not significantly associated with odds of favorable outcomes (OR, 0.40; 95% CI, 0.13–1.25; p = .12).	Low

PICO 1. Timing of Mobilization and Mortality and Functional Recovery After Ischemic Stroke *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Poletto, 2015	37	Pilot RCT	Ischemic stroke	To evaluate the safety and feasibility of EM (within 48 hours of stroke) compared with usual care	The percentage of those with a favorable mRS score (0–2) at 3 months was similar between the EM (50%) and control groups (53%; $p = 0.87$). Mortality rates were similar between groups (13% vs. 12%; $p = 0.68$).	Low
Tong, 2019	284	Pilot RCT	Ischemic stroke	To compare early routine mobilization (<1.5 hours/day out of bed within 24–48 hours of stroke onset), early intensive mobilization (EIM; ≥3 hours/day within 24–48 hours of stroke onset), and very early intensive mobilization (VEIM; ≥3 hours/day within 24 hours of stroke onset) on mRS scores at 3 months after stroke	The percentage of those with a favorable mRS score (0–2) at 3 months was statistically significantly greater in the EIM group compared to the VEIM group (53.5% vs. 37.8%; $p = .041$). There were no significant differences observed between the other groups.	Low
Chippala, 2016	86	RCT	All stroke	To evaluate the effect of VEM (within 24 hours of stroke onset) on functional status following acute stroke	At 3-month follow-up, more patients in the intervention group were independent in activities of daily living compared to the standard care group (85% vs. 45%; $p<.01$).	Very low

PICO 2. Impact on Hospital and Functional Outcomes in Critically Ill Patients with Neurological Insult

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Hester, 2017	2,645	Retrospective review	Neuro ICU (mixed diagnoses)	To investigate a progressive mobility program in a neurocritical care population with the hypothesis that the benefits and outcomes of the program (e.g., decreased length of stay) would have a significant positive economic impact	ICU length of stay decreased from 6.5 to 5.8 days in the immediate postimplementation period and was sustained at 5.9 days over the 2-year period ($F_{(2, 2641)} = 3.1$; $p = .045$). Hospital length of stay was reduced from 11.3 to 8.6 days and sustained at 8.8 ±9.3 days ($F_{(2, 2641)} = 13.0$; $p<.001$). The rate of hospital acquired infections decreased by 50% ($p = .607$). The average cost per patient decreased by 16% from the preintervention baseline and an 11% reduction was sustained over 2 years ($F_{(2, 2641)} = 3.1$; $p = .045$). Fall, inadvertent line removal, and 30-day readmission rates did not change significantly.	Moderate
Karic, 2017	171	Quasi-experimental	Aneurysmal subarachnoid hemorrhage (aSAH)	To evaluate the effect of early rehabilitation and mobilization on complications during the acute phase and within 90 days after aSAH	Patients in the early rehab group reached a higher mobilization level at discharge than those in the control group (Step 5 vs. Step 4; $p = .004$). No patients suffered accidental falls or had episodes of unintended device removal. There was significantly less clinical vasospasm in the early rehab group (14% vs. 29%; $p = .03$). There was >30% risk reduction in severe vasospasm for each step of mobilization achieved during the first 4 days after aneurysm repair. Length of stay (intervention: 13.9 [3–37], control: 14.5 [2–61]; $p>.05$) and rates of respiratory tract infections (intervention: 54%, control: 58%; $p>.05$), DVT (2 in both groups), PE (intervention: 2, control: 1), and rebleeding (0 in both groups) were similar between both groups.	Moderate

PICO 2. Impact on Hospital and Functional Outcomes in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Kinoshita, 2017	227	Prospective observational	Ischemic/ hemorrhagic stroke	To compare the effects of a PROr program applied within 24, 24–48, and >48 hours for acute stroke during a short-term hospital stay (2–3 weeks)	Hospital length of stay was significantly shorter in the VEM group compared with the later group (14.2±1.1 vs. 19.5±1.1; $p<.05$). The GCS scores at hospital discharge were significantly greater in the VEM group compared with the EM or later groups ($p<.05$), but the gains in GCS scores did not significantly differ among the three groups (VEM: 0.9±0.2, EM: 0.7±0.2, later: 1.2±0.2; $p>.05$). Gains in total FIM and motor subscale scores were significantly greater in the VEM group compared with the other two groups (Total FIM: VEM: 32.6±3.0, EM: 20.2±2.3, later: 19.9±2.2; $p<.001$; Motor subscale: VEM: 28.5±2.7, EM: 17.7±2.1, later: 15.9±1.8; $p<.001$). There were no significant differences among the three groups with regard to mortality (VEM: 4.3%, EM: 5.2%, later: 6.8%; $p>.05$).	Moderate
Schaller, 2019	200	Secondary analysis of RCT	Surgical ICU	To assess the effectiveness of early, goal-directed mobilization in critically ill patients across a broad spectrum of initial consciousness levels	There was no evidence that early, goal-directed mobilization affected functional independence at discharge as evaluated by immediate postrandomization GCS scores (likelihood ratio test: $p = .40$; general linear modeling: $p = .53$). In subgroup analyses, EM significantly increased functional independence at hospital discharge in patients with both low and high GCS scores (GCS ≤ 8: OR, 3.67; 95% CI, 1.02–13.14; $p = .046$; GCS > 8: OR, 2.29; 95% CI, 1.11–4.71; $p = .025$).	Moderate

PICO 2. Impact on Hospital and Functional Outcomes in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Bartolo, 2017	103	Prospective observational	Severe acquired brain injury (traumatic and nontraumatic)	To determine whether EM of patients with severe acquired brain injury, performed in the intensive/neurointensive care unit, influenced functional outcome	Both groups showed significant improvement in GCS, Disability Rating Scale, Level of Cognitive Functioning Scale, and early rehabilitation Barthel Index (ERBI) scores. The mobility group showed significantly greater improvements in FIM cognitive (p = .04), GCS (p = .004), and ERBI (p = .005) scores. Rates of discharge to rehabilitation were significantly higher for the mobility group (27.9%) than the no mobility group (0%) (p<.001). Patients in the mobility group stayed longer in the ICU (p = .01). In-hospital mortality did not differ between groups (mobility: 10.3%, no mobility: 17.1%; p = .357). The incidence of pressure injuries was significantly higher in the mobility group (27.1% vs. 9.4%; p = .047).	Low
Young, 2019	56	Prospective observational	SAH	To compare the safety of a nurse-driven EM approach for patients with SAH and EVD compared to a physical therapist/occupational therapist–guided mobilization approach	ICU length of stay was lower using the nurse-driven protocol vs. the physical therapist/occupational therapist–driven protocol (16.1 days vs. 18.7 days; p = .007). Discharge disposition significantly improved compared to standard care (OR, 3.83; 95% CI, 1.14–9.16; p < .001).	Low
Olkowski, 2015	93	Retrospective review	aSAH	To determine whether an EM program for patients with aSAH has an effect on function and hospital length of stay	Patients in the EM group participated in out-of-bed activity 2.2 days earlier (p = .039), walked 50 feet 4.1 days earlier (p = .004), and were discharged from the hospital 2.9 days earlier (p = .015). The number of patients discharged to the community did not differ significantly between groups (EM: 60%, control: 50%; p = .481).	Low
Mulkey, 2014	228	Quasi-experimental	Neuro ICU (mixed diagnoses)	To assess patient characteristics and clinical outcomes of patients treated in a neuro ICU based on greatest level of mobility achieved	Length of stay varied between groups, although those who achieved greater mobility levels tended to have a longer length of stay (p < .001); discharge to home was associated with greater mobility status (p < .001).	Low
Saciri, 2002	59	Prospective observational	aSAH	To analyze functional and cognitive outcomes in patients receiving early rehabilitation treatment after surgery for aSAH	At discharge, 72.7% of patients were without motor impairment, but 59.6% showed cognitive impairment; 43.4% (n = 23) of patients had attained independence in activities of daily living.	Low

PICO 2. Impact on Hospital and Functional Outcomes in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Witcher, 2015	68	Retrospective review	Neuro ICU (mechanically ventilated; mixed diagnoses)	To investigate the impact of an EM program on sedative and analgesic use, duration of mechanical ventilation, and hospital and ICU length of stay	There was a significant increase in total cumulative opioid dose during the ICU stay in the pre-EM versus post-EM groups (50.0 ug/d vs. 173 ug/d; p = .012). The cumulative doses of benzodiazepines, propofol, and dexmedetomidine were not statistically different between groups. The proportion of patients managed with antipsychotic agents during their ICU stay did not differ between groups (25.8% vs. 12.5%; p = .230). The duration of mechanical ventilation (5 [3–18] days vs. 7 [4–19] days; p = .720), hospital length of stay (22 [12–34] days vs. 23 [16–35] days; p = .416), and ICU length of stay (10 [6–19] days vs. 13 [8–18] days; p = .188) did not differ between groups. The proportion of patients discharged home did not differ between groups (9.7% vs. 5.4%; p = .653).	Low
Klein, 2015	637	Prospective observational	Neuro ICU (mixed diagnoses)	To determine if an EM protocol increased mobility and improved clinical and psychological outcomes	In the postintervention group, there was a two-fold increase in the percentage of patients who were able to achieve weight-bearing status, pivot to a chair, or walk during the ICU stay (42.7% vs. 21.2%; p<.001). Hospital and ICU length of stay was significantly shorter in the postintervention group (both p<.001). The prevalence of bloodstream infections was reduced by 3% (p = .015) and the prevalence of hospital-acquired pressure injury was reduced by 2.7% (p = .026). There were no differences between groups in 30-day mortality, ventilator-associated pneumonia, or DVT. Postintervention, patients experienced lower anxiety scores (p = .029), but depression and hostility did not change from the pre- to postintervention period.	Low

PICO 2. Impact on Hospital and Functional Outcomes in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Bahouth, 2018	57	Quasi-experimental	ICH	To measure the impact of a progressive mobility program on patients admitted to a neurocritical care unit with ICH	Patients in the postintervention group were not more likely to be mobilized on day 1 of their neurocritical care unit stay (OR, 1.5; 95% CI, 0.2–11.7; $p = 0.67$) but were more likely to be mobilized within 7 days (OR, 8.7; 95% CI, 21–36.6; $p = .003$). There were no reported episodes of hypotension, change in neurological status, falls, or line dislodgements. There were no statistically significant differences between groups on mortality (4% vs. 24%; $p = .12$), ICU length of stay (4.5 vs. 6.1 days), hospital length of stay (11.0 vs. 11.3 days), or number of patients discharged home (43% vs. 38%; $p = .12$).	Low
Guclu-Gunduz, 2012	124	Prospective observational	Ruptured/ unruptured cerebral aneurysm	To analyze outcomes in patients with SAH who received early physiotherapy after surgical clipping or endovascular embolization of a cerebral aneurysm	Functional status (measured by Barthel Index) significantly improved in the groups who underwent surgical aneurysm clipping. Patients with low-grade SAH (Hunt Hess grade I or II) who underwent surgical clipping or endovascular embolization had better functional outcomes than groups with higher-grade SAH. There was no significant difference in hospital length of stay ($p>.05$).	Very low
Moyer, 2017	45	Prospective observational	SAH	To assess the feasibility, safety, and outcome of an early mobility protocol for patients with SAH with an EVD	More patients in the intervention group were discharged to home/acute rehab (88.5% vs. 57.9%; $p = .018$); all other outcome variables (ICU length of stay, hospital length of stay, ventilator days, tracheostomy placement, restraint days) were similar between groups.	Very low
Yataco, 2019	153	Retrospective review	Patients with EVD	To describe the outcomes and adverse events of first mobilization attempt in neurosurgery patients with EVD who participated in early functional mobilization with physical therapy or occupational therapy	Median time from EVD placement to initial mobilization was 38 hours (range, 4–537); 51 patients (43.6%) achieved ambulation. Adverse events were rare and transient (6.9%; 95% CI, 3.5%–12.9%). No EVD dislodgement occurred.	Very low

PICO 3. Impact on Patient Safety Events in Critically Ill Patients with Neurological Insult

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Bernhardt, 2008	71	RCT	Ischemic/ hemorrhagic stroke	To compare mortality and functional outcome at 3 months after stroke between a VEM and usual care group	More patients in the VEM group died (8 vs. 3; absolute risk difference = 12.0%; 95% CI, -4.3% to 28.2%; p = .20). This difference did not remain after adjusting for baseline stroke severity and premorbid mRS scores. The total number of adverse events at 3 months was similar between groups (VEM: 15, usual care: 14; p = .846). There was no difference in fall rates between groups during the intervention period (VEM: 19.7; 95% CI, -2.1 to 41.4; usual care: 22.8; 95% CI, 0.4 to 45.3; p = .81). There was no difference in deterioration between groups from day 0 to day 7 (VEM: 8, usual care: 9; p = .78).	High
Langhorne, 2010	32	RCT	Ischemic/ hemorrhagic stroke	To compare conventional stroke unit procedures with more progressive (nurse-led) protocols of early mobility and/ or automated physiological monitoring	There were no significant safety concerns.	High
Karic, 2017	37	Prospective observational	aSAH	To describe and quantify the content of early rehabilitation adapted to patients with acute aSAH and assess its feasibility	No serious adverse effects were observed.	Moderate
Hester, 2017	2,645	Retrospective analysis	Neuro ICU (mixed diagnoses)	To investigate a progressive mobility program with the hypothesis that the benefits and outcomes of the program would have a significant positive economic impact	Hospital-acquired infections decreased by 50% (p = .607). Average cost per patient decreased by 16% from preintervention baseline, and an 11% reduction was sustained over 2 years ($F_{(2, 2641)}$ = 3.1; p = .045). Fall rates, inadvertent line removal, and 30-day readmissions did not change significantly.	Moderate
Adeolu, 2012	50	Observational	Subdural hematoma	To evaluate the efficacy and complications of each type of mobilization following burr-hole drainage of subacute and chronic subdural hematoma	Two complications occurred in the late mobilization group (one wound infection, one tension pneumocephalus). No recurrence or problems were associated with prolonged bed rest in the two groups.	Low
Diserens, 2012	42	Pilot RCT	Ischemic stroke	To evaluate whether EM after acute ischemic stroke is better than delayed mobilization with regard to medical complications, neurological function, and cerebral blood flow	There were no differences between groups in the total number of complications or in clinical outcomes.	Low

PICO 3. Impact on Patient Safety Events in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Sundseth, 2012	56	RCT	All stroke	Primary outcome: to identify and compare the proportion of poor outcome at 3 months poststroke Secondary outcomes: to identify mortality rate at 3 months, change in neurological impairment, dependency in activities of daily living, and type and number of all complications within 3 months after stroke	VEM had nonsignificant greater odds of poor outcome (adjusted OR, 2.70; 95% CI, 0.78–9.34; $p = 0.73$) and mortality (OR, 5.26; 95% CI, 0.84–32.88; $p = 0.08$), and dependency (OR, 1.25; 95% CI, 0.36–4.34; $p = 0.73$).	Low
Titsworth, 2012	170	Observational	Neuro ICU (mixed diagnoses)	To investigate the effectiveness of increased mobility among neuro ICU patients	Initiation of this protocol correlated with reduced hospital-acquired infections (5.5±0.9 vs. 2.2±1.0; $p<.05$), fewer instances of ventilator-associated pneumonias (2.14±0.95 vs. 0±0; $p<.001$), and decreased number of restraint-days (368.57±46.8 vs. 301.2±55.3; $p<.05$). Increased mobility did not lead to significant changes in fall rates (1.39±0.57 vs. 1.31±0.85; $p = .867$), critical line pulls (0.90±0.53 vs. 0.67±0.81; $p = .63$), or acquired pressure injuries (2.6% vs. 4.6%; $p = .22$).	Low
Olkowski, 2013	25	Retrospective analysis	aSAH	To determine the safety and feasibility of an EM program for patients with aSAH	Adverse events occurred in 5.9% of EM program sessions, all because of hemodynamic changes.	Low
Klein, 2015	637	Prospective observational	Neuro ICU (mixed diagnoses)	To determine if an EM protocol increased mobility and improved clinical and psychological outcomes	The postintervention cohort had fewer bloodstream infections and hospital-acquired pressure injuries and less anxiety (all $p<.03$). There were no significant differences in ventilator-associated pneumonia or DVT.	Low
Olkowski, 2015	93	Retrospective analysis	aSAH	To examine the effects of an EM program on patients with aSAH	Patients in the EM group participated in out-of-bed activity 2.2 days earlier ($p = .039$), walked 50 feet 4.1 days earlier ($p = .004$), and were discharged from the hospital 2.9 days earlier ($p = .015$).	Low

PICO 3. Impact on Patient Safety Events in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Witcher, 2015	68	Retrospective analysis	Neuro ICU (mixed diagnoses)	To determine whether there would be a decrease in sedative and analgesic use as well as a decrease in the duration of mechanical ventilation, hospital length of stay, and ICU length of stay after implementation of an EM program	There was a significant increase in the total cumulative opioid dose during the ICU stay in the pre-EM vs. post-EM groups (50.0 ug/d vs. 173 ug/d; $p = .012$). The cumulative doses of benzodiazepines, propofol, and dexmedetomidine were not statistically different between groups. The proportion of patients managed with antipsychotic agents during their ICU stay did not differ between groups ($p = .230$). The duration of mechanical ventilation (5 [3–18] days vs. 7 [4–19] days; $p = .720$), hospital length of stay (22 [12–34] days vs. 23 [16–35] days; p = .416), and ICU length of stay (10 [6–19] days vs. 13 [8–18] days; $p = .188$) did not differ between groups.	Low
Rocca, 2016	30	Pilot RCT	Neuro ICU and intermediate care unit (mixed diagnoses)	To observe and quantify changes in sympathetic activity and blood pressure during gradual postural changes by the verticalization robot and after training by a lower-body ergometer	No significant differences in blood pressure were seen between the three groups. The analysis of catecholamines suggested a significant increase in catecholamine production using standard mobilization with physiotherapists and MOTOmed letto and no changes with Erigo.	Low
Bartolo, 2017	103	Prospective observational	Severe acquired brain injury (traumatic and nontraumatic)	To determine whether EM of patients with severe acquired brain injury, performed in the intensive/neuro intensive care unit, influences functional outcomes	No mobilization-related adverse events were reported. The incidence of pressure sores was significantly greater in the mobility group (27.1% vs. 9.4%; $p = .047$).	Low
Bahouth, 2018	57	Quasi-experimental	ICH	To measure the impact of a progressive mobility program on patients admitted to a neurocritical care unit with ICH	No neurological deterioration, hypotension, falls, or line dislodgements were reported in association with mobilization.	Low
Shah, 2018	90	Prospective observational	Patients with EVD	To determine the safety and feasibility of EM in patients with EVDs	There were four (2.2%) adverse events recorded during the entire study.	Low
Yataco, 2019	117	Retrospective analysis	Patients with EVD	To describe the outcomes and adverse events of the first mobilization attempt in neurosurgery patients with EVD	No major safety events occurred. Transient adverse events (i.e., headache, nausea, transient diastolic blood pressure elevation) occurred 6.9% of the time, with no permanent neurological sequelae.	Low
Young, 2019	56	Prospective observational	SAH	To determine whether a nurse-driven mobilization protocol would result in safe and more frequent mobilization than institutional standard care	No adverse events were attributable to EM.	Low

PICO 3. Impact on Patient Safety Events in Critically Ill Patients with Neurological Insult *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Naito, 2020	407	Retrospective analysis	Ischemic/ hemorrhagic stroke	To examine the associations between out-of-bed mobilization (OM) and complications of immobility	The total complication rates of immobility, pneumonia, and pressure injury were significantly lower in the OM group than in the bed rest group (Total: 60.7% vs. 88.5%, $p<.05$); pneumonia: 45.5% vs. 65.5%, $p<.01$; pressure injury: 3.6% vs. 12.5%, $p<.01$). No differences between incidence of urinary tract infection or falls were observed (urinary tract infection: 8.3% vs. 11.5%, $p = .31$; falls: 3.3% vs. 1.9%, $p = .47$).	Low
Frazzitta, 2015	4	Observational	Traumatic brain injury	To evaluate the feasibility and safety of the very early use of a tilt table with stepping device	No adverse events occurred during all treatments, and there were no interrupted sessions. Hemodynamic parameters stayed within the predefined safety range during all procedures. No changes in neurological status appeared during the sessions.	Very Low
Booth, 2016	343	Observational	Neuro trauma ICU (mixed diagnoses)	To compare ICU trauma patient outcomes before and after implementation of a structured progressive mobility protocol	There were no significant differences between groups regarding hospital and ICU stay, ventilator days, mortality, falls, respiratory failure, or instances of pneumonia. The postintervention cohort had a statistically significantly lower incidence of venous thromboembolism than the preintervention cohort (7.5% vs. 21%; $p = .0004$).	Very Low
Moyer, 2017	45	Prospective observational	SAH	To determine the safety, feasibility, and outcome of an EVD mobilization protocol in patients with SAH	Six mobilization sessions were aborted because of increased lethargy, pain, increased intracranial pressure, drain malfunction, and hypotension.	Very Low

PICO 4. Effect on Safety Events and Functional Outcomes in the Acute Rehabilitation Setting

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Franceschini, 2018	310	Observational	Ischemic/ hemorrhagic stroke	To assess early poststroke prognostic factors in patients admitted for postacute phase rehabilitation	EM in <48 hours was significantly associated with better outcomes in performance of daily activities (OR, 2.306; 95% CI, 1.127–4.723; p = .022), whereas mobilization in <72 hours was not.	Moderate
Yadav, 2018	30	RCT	Ischemic/ hemorrhagic stroke	To determine the efficacy of a 1-month exercise program using a robotic tilt table versus conventional physiotherapy treatment in the rehabilitation of patients with hemiplegia following stroke	After 30 days, both groups showed an improvement in quality of life and muscle strength. Participants in the intervention group showed more improvement overall in all domains. No adverse events were reported.	Moderate
Mohan, 2013	22	Pilot RCT	Ischemic/ hemorrhagic stroke	To evaluate the effectiveness of mirror therapy on lower extremity motor recovery, balance, and mobility in patients with acute stroke	All outcome parameters improved significantly in both groups after treatment. Between groups, the change score of Functional Ambulation Categories showed more improvement in the mirror group than in the control group. No adverse events were observed.	Low
Tang, 2014	48	RCT	Ischemic/ hemorrhagic stroke	To determine whether subjects with severe motor deficit after stroke who received early CBA (ECBA) would achieve higher motor and balance scores than subjects who received CBA alone.	Overall Stroke Rehabilitation Assessment of Movement (STREAM) and balance scores were higher in the ECBA group after 8 weeks of therapy (p<.001 for both). The change in STREAM scores was significantly greater in the ECBA group than in the CBA group after 8 weeks of therapy (p<.001). There was no difference in upper extremity mobility between groups. No falls or other adverse events were reported.	Low
Krewer, 2015	50	RCT	Neurological rehabilitation hospital (mixed diagnoses)	To evaluate the effectiveness of a tilt table therapy with or without an integrated stepping device on level of consciousness	The Coma Recovery Scale–Revised scores improved for the tilt table with stepping group. The rate of recovery for the group treated with conventional tilt table therapy significantly increased during treatment. Changes in spasticity did not differ between groups. Therapy interruptions were significantly more frequent in the tilt table with stepping group (p<.001).	Low

PICO 5. Impact of Early Versus Delayed Mobilization on Hospital Outcomes and Safety Events in Acute Ischemic Stroke Patients Who Receive IV Thrombolysis

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Langhorne, 2010	32	Pilot RCT	Ischemic/ hemorrhagic stroke	To compare conventional stroke unit procedures with more progressive protocols of early activity mobilization and/ or automated monitoring	The EM patients were significantly more likely to achieve walking by day 5 and were less likely to develop complications of immobility. There were no significant safety concerns.	High
Bernhardt, 2015	2,104	RCT	Ischemic/ hemorrhagic stroke	To compare the effectiveness of frequent, higher-dose, VEM with usual care after stroke	Odds of favorable outcome (mRS 0–2): adjusted OR, 0.73; 95% CI, 0.59–0.90; p = .004	High
Langhorne, 2017	2,104	RCT	Ischemic/ hemorrhagic stroke	To evaluate the effectiveness of frequent, high-dose VEM after stroke	At 3-month follow-up, fewer patients in the VEM group had a favorable outcome than the usual care group (adjusted OR, 0.73; 95% CI, 0.59–0.90; p = .004). Subgroup analyses tended to favor the usual care intervention, with poorest outcomes in the population with ICH undergoing VEM, although no findings reached statistical significance (p > .05).	High
Kinoshita, 2017	227	Observational	Ischemic/ hemorrhagic stroke	To compare the utility of PROr applied early or late after acute stroke	The overall mortality rate was 5.7%, including two patients (4.3%) in the VEM group. GCS scores improved significantly during the hospital stay for all three groups, but improvement on discharge was significantly better in the VEM group. FIM scores improved significantly in all three groups, but gains in total FIM and motor subscale scores were significantly greater in the VEM group.	Moderate
Herisson, 2016	138	RCT	Ischemic stroke	To test the hypothesis that early sitting could be beneficial to stroke patient outcomes	There was no difference in the proportion of patients in each group with an mRS score of 0–2 at 3 months (30.7% vs. 25%; p = .52); 3-month Barthel Index scores were significantly higher in the early sitting group (96.67±8.09 vs. 90.53±22.28; p = .05).	Moderate
Bernhardt, 2008	71	RCT	Ischemic/ hemorrhagic stroke	To compare mortality and functional outcome at 3 months	More patients in the VEM group died (8 vs. 3; absolute risk difference = 12.0%; 95% CI, -4.3% to 28.2%; p = .20). This difference did not remain after adjusting for baseline imbalance in stroke severity and premorbid mRS scores. The total number of serious adverse events at 3 months was similar between groups (p = .846). There was no difference in fall rates between groups during the intervention period (p = .78).	Low

PICO 5. Impact of Early Versus Delayed Mobilization on Hospital Outcomes and Safety Events in Acute Ischemic Stroke Patients Who Receive IV Thrombolysis *(continued)*

First Author, Year	Sample Size	Study Design	Sample Population	Study Aim(s)	Results	Quality
Sorbello, 2009	71	Secondary analysis of RCT	Ischemic/ hemorrhagic stroke	To compare VEM with standard stroke unit care	There were no significant group differences in the number, type, or severity of complications by 3 months. Most patients (81.6%) experienced one or more complications. Falls were common.	Low
Sundseth, 2012	56	RCT	Ischemic/ hemorrhagic stroke	Primary outcome: to compare the proportion of poor outcome (mRS score 3–6) between a VEM and a control group. Secondary outcome: mortality	The VEM group had nonsignificant higher odds of poor outcomes (adjusted OR, 2.70; 95% CI, 0.78–9.34; p = 0.73), mortality (OR, 5.26; 95% CI, 0.84–32.88; p = 0.08), and dependency (OR, 1.25; 95% CI, 0.36–4.34; p = 0.73).	Low
West, 2013	146	Prospective observational	Ischemic/ hemorrhagic stroke	To test the hypothesis that rehabilitation focus in the comprehensive stroke unit (versus an acute stroke unit) promotes early physical activity and discharge directly home	The comprehensive stroke unit spent 14.4% more time in moderate to high levels of activity (95% CI, 8.9%–19.8%; p<.001) and 18.5% less time physically inactive (95% CI, 5.0%–32.0%; p = .008) and were more likely to be discharged directly home (OR, 3.7; 95% CI, 1.4–9.5; p = .007).	Low
Poletto, 2018	37	Pilot RCT	Ischemic stroke	To evaluate the feasibility, safety, and benefits of EM	No complications (symptomatic hypotension or worsening neurological symptoms) were associated with EM. Rates of pneumonia, PE, DVT, and mortality were similar in both groups.	Low
Silver, 2020	392	Prospective observational	Ischemic stroke	To compare discharge outcomes, rates of pneumonia and venous thromboembolism, and length of stay in patients who had ≥24 hours versus ≥12 hours of bed rest following stroke thrombolysis	Those in the ≥12-hour bed rest group had a shorter average length of stay than the ≥24-hour bed rest group (3.5 vs. 5.4 days; p = 0.006) and lower incidence of pneumonia (3 vs. 17; p = 0.006). Discharge outcomes (p = .50) and venous thromboembolism events (p = .310) were the same between groups.	Low

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