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## Early mobilization in acute stroke phase: a systematic review

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### ABSTRACT

**Background:** Early mobilization is defined as out-of-bed activities in acute stroke phase, and has led to improvements in functional capacity and reduction of complications after stroke.

**Objective:** This study aimed to investigate the effectiveness and safety of early mobilization in the acute stroke phase.

**Methods:** This was a systematic review. We searched for studies with the keywords: "Stroke," "Early mobilization" and "Functional outcomes." Data source: NLM, LILACS, MEDLINE, PEDro, and Science Direct. Studies published up to June 2020 were included; (b) study eligibility criteria: clinical trials; (c) participants: stroke patients in the acute phase; (d) interventions: early mobilization; (e) study appraisal: two authors independently assessed the risk of bias, Grading of Recommendations Assessment, Development and Evaluation, and the Oxford Center for Evidence-Based Medicine Levels of Evidence. The safety was evaluated based on related and non-related adverse effects.

**Results:** Altogether, 476 studies were retrieved. After exclusion, seven studies involving 8663 patients were included in the qualitative synthesis. The main activities were elevation of the headboard, sitting, standing, and walking. The most important outcome assessed was the modified Rankin scale score (disability) after 3 months of stroke, and two studies showed that early mobilization improves functional capacity after stroke.

**Conclusion:** the optimal time to start early mobilization is > 24 h of stroke according to hemodynamic stability and safety criteria. The duration of mobilization is recommended between 15 and 45 minutes, divided into one, two, or three times a day. The focus of early mobilization should be on sitting, standing, and walking activity.

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### KEYWORDS

Stroke; ischemic stroke; rehabilitation; early mobilization; physical therapy

## Introduction


Stroke is characterized by sudden neurological deficit of vascular origin and is currently considered the main cause of chronic disability in adults.<sup>1,2</sup> Mortality in stroke patients has decreased in recent decades due to greater control of risk factors and improvements in care services. However, stroke negatively affects the performance of activities of daily living and can contribute to an increase in the incidence of mortality and morbidity in the long-term.<sup>3,4</sup>

Stroke is ranked as the second leading cause of death worldwide with an annual mortality rate of about 5.5 million, and main cause of chronic disability in adults.<sup>5–7</sup> There has been an increase in the number of patients with disabilities after stroke,

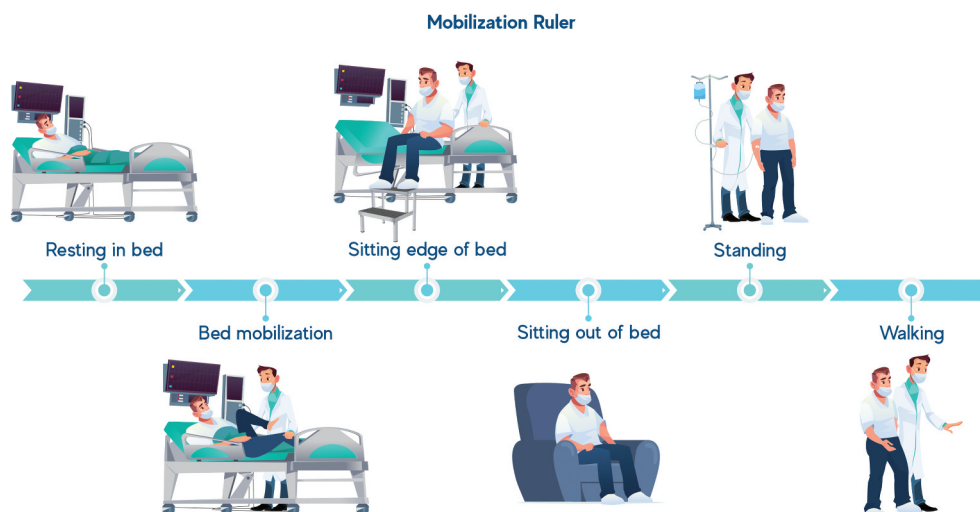
and early multidisciplinary care is essential to increase their chances of returning to social life and their daily activities.<sup>1,8</sup> Several studies have demonstrated that early quality care, especially by a multidisciplinary stroke team during the acute phase, reduces the levels of functional disability in the long term (Figure 1).<sup>9,10,11</sup>

During the first 24 h after stroke, the multidisciplinary stroke team should be attentive to clinical stabilization. However, after this period, immobility is known to be a major cause of death in patients who had their first stroke. Bed immobilization can result in pneumonia, deep venous thrombosis, reduced muscle mass, joint limitation, and dysfunctions of the cardiovascular and cardiorespiratory system, and this limits rehabilitation.<sup>12</sup>

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**Figure 1.** Hospital protocol for early mobilization.



**Figure 2.** Flow chart for early and intensive mobilization out of bed in acute stroke phase

**Table 1.** Key terms and MeSH strategy employed during the literature review.

PICO Process	Keyword/Mesh
(P) Population	<i>Stroke OR Ischemic Stroke OR Strokes OR Cerebrovascular Accident OR Cerebrovascular Accidents OR CVA (Cerebrovascular Accident) OR CVAs (Cerebrovascular Accident) OR Cerebrovascular Apoplexy OR Brain Vascular Accident OR Brain Vascular Accidents OR Cerebrovascular Stroke OR Cerebrovascular Strokes OR Apoplexy OR Cerebral Stroke OR Cerebral Strokes OR Acute Strokes OR Acute Cerebrovascular Accident OR Acute Cerebrovascular Accidents OR Hemorrhagic Stroke OR Subarachnoid Hemorrhagic Stroke OR Subarachnoid Hemorrhagic Strokes OR Intracerebral Hemorrhagic Strokes OR Intracerebral Hemorrhage Stroke OR Intracerebral Hemorrhage Strokes</i>
(I) Intervention	<i>Early mobilization OR early rehabilitation OR rehabilitation OR habilitation</i>
(C) Control	<i>Any comparison</i>
(O) Outcome	<i>Disability Evaluations OR Disability Evaluation OR Functional status OR Status, Functional OR Functional Independence OR Independence, Functional OR Functional Dependence OR Activities of Daily Living OR ADL OR Activities, Daily Living OR Activity, Daily Living OR Daily Living Activities OR Daily Living Activity OR Living Activities, Daily OR Living Activity, Daily OR Limitation of Activity, Chronic OR Chronic Limitation of Activity OR adverse events OR side effects</i>

However, it is still unclear in the literature whether mobilization within 24 hours of the ictus can contribute to a decrease in cerebral blood flow due to the blood pressure variability of the acute phase.<sup>13</sup> Therefore, mobilizations during the acute phase of a stroke have prophylactic goals,<sup>14</sup> which include improving cardiovascular fitness and preventing muscle loss.

However, controversies remain regarding the safety and benefits of the early mobilization in acute stroke phase.<sup>15–19</sup> Currently, admissions to stroke units have facilitated the development of effective treatment protocols, and early mobilization has been systematically used to reduce the number of complications and improve functional capacity.<sup>20,21</sup> However, the onset time for early mobilization after stroke, the type of activity or exercise, as well as the frequency (sessions/day), session time (minutes), safety criteria and dose (intensity) used are still under debate in the literature. Therefore, this study aimed to investigate the effectiveness and safety of early mobilization in the acute stroke phase. In addition, we developed a hospital protocol for early mobilization during the acute phase of stroke based on the main results.

## Methods

### Protocol and registration

We followed the methods described in the Cochrane Handbook for Intervention Reviews. Our review also followed the items recommended by the Systematic Review Protocol checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).<sup>22</sup> This review was conducted in accordance with the international prospective registry of systematic reviews (PROSPERO, number xxx).

### Eligibility criteria

The eligibility criteria were as follows:

- Participants: Individuals with clinical and neuroimage confirmation of stroke;
- Interventions: Early mobilization and early rehabilitation such as out-of-bed sitting, standing, and walking activities during the acute phase of stroke (i.e. within the first 24 to 72 hours).<sup>23</sup>
- Control: Any comparison;
- Outcomes: All impairments were considered (sensory-motor function, cognition, language, balance, and locomotion), functional recovery (follow-up), and treatment safety (related and non-related side effects in the short and long-term outcomes).
- Study design: Randomized, quasi-randomized, and non-randomized clinical trials

### Information sources

The following electronic databases were searched: National Library of Medicine (NLM), Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE), Physiotherapy Evidence Database (PEDro), and Science Direct.

### Other research sources

To identify additional published, unpublished, and ongoing trials, we:

- screened the reference lists of the identified studies.
- contacted the study authors and experts
- used the Science Citation Index Cited Reference Search to track important articles.

**Table 2.** Characteristics of included studies.

Author/ Year	Country	Study design	Number of participants	Outcomes	Intervention	GRADE	PEDRO	OXFORD
AVERT Trial Collaboration group (2015) <sup>26</sup>	Australia, New Zealand, Malaysia, Singapore, United Kingdom	Pragmatic, parallel-group, single-blind, multicentre, international, randomized controlled trial	Control: 1050 Intervention: 1054 56 Stroke Units	Primary: mRS 3 months Secondary: time taken to achieve unassisted walking over 50 m; deaths and serious adverse events at 3 months.	Control: usual care Intervention: mobilization begin within 24 h; focus on sitting, standing, and walking (ie, out-of-bed) activity	High	8	2
Bernhardt (2016) <sup>27</sup>	Australia, New Zealand, Malaysia, Singapore, United Kingdom	Pragmatic, parallel-group, single-blind, multicentre, international, randomized controlled trial	Control: 1050 Intervention: 1054 56 Stroke Units	Primary: mRS 3 months Secondary: Frequency of activities	Control: usual care Intervention: mobilization begin within 24 h; focus on sitting, standing, and walking (ie, out-of-bed) activity	High	8	2
Chippala (2016) <sup>28</sup>	India	Single-blind, randomized controlled trial	Control: 40 Intervention: 40 Units	Primary: Functional status – Barthel index 3 months	Control: usual care Intervention: mobilization begin within 24 h; focus on standing (ie, out-of-bed) activity	Moderate	7	2
Cumming (2018) <sup>29</sup>	Australia, New Zealand, Malaysia, Singapore, United Kingdom	Pragmatic, parallel-group, single-blind, multicentre, international, randomized controlled trial	Control: 1050 Intervention: 1054 56 Stroke Units	Primary: mRS at 3 months Secondary: Cognitive function	Control: usual care Intervention: mobilization begin within 24 h; focus on sitting, standing, and walking (ie, out-of-bed) activity	High	8	2
Herisson (2016) <sup>30</sup>	France	Parallel-group, single-blind, multicentre, randomized controlled trial	Control: 75 Intervention: 63 11 Stroke Units	Primary: mRS at 7 days and 3 months	Day 0: headpost position 30–45°, Day 1: 60° + sitting. Day 2: standing.	Moderate	7	2
Langhorn (2017) <sup>17</sup>	Australia, New Zealand, Malaysia, Singapore, United Kingdom	Pragmatic, parallel-group, single-blind, multicentre, international, randomized controlled trial	Control: 1050 Intervention: 1054 56 Stroke Units	Primary: mRS at 3 months Secondary: mRS at 12 months	Control: usual care Intervention: mobilization begin within 24 h; focus on sitting, standing, and walking (ie, out-of-bed) activity	High	8	2
Polleto (2015) <sup>31</sup>	Brazil	Single-blind, randomized controlled trial	Control: 15 Intervention: 14 Units	Primary: safety and feasibility of early mobilization within 48 hours	Sitting, standing, and walking (ie, out-of-bed) activity and Bobath concept	Low	7	2

GRADE classification: • High-quality evidence: Findings are consistent among at least 75% of the RCTs with a low risk of bias; data are consistent, direct, and precise, and no publication biases are known or suspected. Additional research is unlikely to change the estimate or our confidence in the results; • Moderate-quality evidence: One of the domains is not met. Additional research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; • Low-quality evidence: Two of the domains are not met. Additional research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; • Very low-quality evidence: Three of the domains are not met. We are very uncertain about the results.

OXFORD classification: Level 1: Systematic review of randomized trials or n-of-1 trials; Level 2: Randomized trial or observational study with dramatic effect; Level 3: Non-randomized controlled cohort/follow-up study; Level 4: Case-series, case-control studies, or historically controlled studies; Level 5: Mechanism-based reasoning

## Search

Table 1 presents the search strategies. Studies published up to June 2020 were included.

## Study selection

Studies involving individuals diagnosed with stroke who were undergoing treatment with early mobilization were included, with outcome endpoints such as sensory-motor function, cognition, language disorders, quality of life, static and gait balance, and treatment safety. The exclusion criteria were as follows: duplicate articles, systematic reviews, unavailable in full articles, chapters, or abstracts, animal or cell-based models, case studies or series case, case-control studies, cross-sectional studies, cohort studies, and off-topics.

Two reviewers independently screened all titles and abstracts of the studies yielded by the literature search, obtained full-text articles of all potentially eligible studies, and evaluated them for eligibility. The reviewers resolved disagreements by discussion or, if necessary, with third-party adjudication. We also considered studies reported only as conference abstracts.

## Selection of studies

The reviewers performed calibration exercises and worked in pairs to extract data independently from the included studies, following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions. They resolved disagreements by discussion or, if necessary, with third-party adjudication. Multiple reports of the same study were collated so that each study (not each reference) was the unit of analysis in the review. The process of selecting the references was recorded and the PRISMA flow diagram was completed.

## Data charting process

Two reviewers independently extracted data from the included studies. A standardized data extraction form was used and the following details were recorded from each study: characteristics of the study population (study year, number of included

participants in the trial, primary and secondary outcomes, protocol of intervention effectiveness, setting, and related or non-related side effects.

## Bias risk assessment

Two authors of this review independently assessed the risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Disagreements were resolved through discussion or consultation with another author. After risk of bias evaluation by Cochrane process, two authors independently assessed the risk of bias for each study, using the criteria described using the PEDro scale (Physiotherapy Evidence Database) to assess bias. Based on the Delphi list developed by Verhagen et al.,<sup>24</sup> the risk of bias was assessed for the following domains: eligibility criteria, randomization and concealment of allocation, similarity between groups and subjects, blinding of therapists and evaluators, percentage of participants who started and continued the study, results for intention to treat, inter-group comparison, and measurement of precision and variability in at least one outcome. The total number of points was 10, and a higher total number of points was associated with a lower risk of bias.

## Evidence recommendation

We summarized the evidence and assessed its certainty separately for randomized controlled trials (RCTs) and non-RCT studies. We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) to rate the certainty of the evidence for each outcome as high, moderate, low, or very low. For the GRADE approach, RCTs begin with high certainty, and non-RCT studies begin with moderate certainty.<sup>22</sup> Detailed GRADE guidelines were used to assess the overall risk of bias, imprecision, inconsistency, indirectness, and publication bias, and to summarize the results in an evidence profile. In addition, the Oxford Center for Evidence-Based Medicine 2011 Levels of Evidence (OCEBM) classification was used, which allows the evaluation of evidence on prevalence, diagnostic accuracy, prognosis, therapeutic effects, rare damage, common damage, and screening.<sup>25</sup>



## Data synthesis

After data extraction, key points were identified in the included studies based on safety, start time, inclusion and exclusion criteria, frequency and type of exercises, and effectiveness of early mobilization. The early mobilization protocol for guiding physiotherapeutic care during the acute phase of stroke was developed by stroke rehabilitation clinicians and other professionals with significant experience in stroke rehabilitation, and it covered various disciplines involved in stroke care. In the first instance, five experts were contacted and invited to participate. They comprised two stroke neurologists, two physical therapists, and one nurse. After the elaboration of the protocol (version 1), all stroke rehabilitation clinicians and other professionals answered questions about the agreement and disagreement between the protocol items (start time, safety criteria, standard evaluation, NIHSS cutoff, type and frequency of mobilization, risk of bias, better recommendations, and level of evidence). When there were agreements between more than 80% of the items, the protocol was finalized (version 2).

## Results

### Study selection

A total of 476 studies were identified. After reading the titles, 93 studies were included in the analysis. The excluded studies during this phase reported mobilization in patients during the chronic phase of stroke. After reading the abstracts, 50 studies were excluded: cross-sectional studies ( $n = 9$ ), cohort studies ( $n = 8$ ), literature review ( $n = 1$ ), duplicate studies ( $n = 32$ ). During this phase, 43 studies were selected for full reading, and 36 studies were excluded because reported mobilization in subacute stroke phase ( $>72$  hours after stroke). Seven studies<sup>17,26–31</sup> that met all the inclusion criteria were included at the end of the review for qualitative analysis.

### Study characteristics

Seven studies were included in the present study. A total of 4333 stroke patients were included in the early mobilization group and 4330 in the control

group. Seven studies were included, with a total of 8663 patients. In five studies,<sup>17,26–29</sup> the intervention protocol was mobilization beginning within 24 h with a focus on sitting, standing, and walking (i.e. out-of-bed) activity. The protocol of one study<sup>30</sup> was as follows: day 0, headpost position 30–45°, day 1: 60°, and sitting; day 2: standing. The protocol of another study<sup>31</sup> was sitting, standing, and walking (i.e. out-of-bed) activity and the Bobath concept.

### Results of individual studies

The AVERT Trial Collaboration group (2015)<sup>26</sup> showed greater efficacy in the control group in relation to the primary outcome (mRS at 3 months); Polleto et al. (2015)<sup>31</sup> showed that early mobilization is feasible and safe in the acute stroke phase; Herisson et al. (2016)<sup>30</sup> showed a significant improvement in mRS at 1 month in the intervention group, but it was not sustained in 3 months; Bernhardt et al. (2016)<sup>27</sup> observed that frequency and activities are significant for the outcome; Chippala and Sharma (2016)<sup>28</sup> showed that early mobilization accelerated the return to activities in 3 months; Langhorn et al. (2017)<sup>17</sup> showed greater efficacy in the control group in relation to the primary outcome; and Cumming et al. (2018)<sup>29</sup> observed no difference between groups based on mRS and cognition. No severe adverse events were observed in any of the studies.

### Synthesis of results

Table 2 presents the main findings of the selected studies. These findings emphasize the importance of early mobilization to improve functionality, quality of life, and return of the patient to basic activities previously performed. The main activities were elevation of the headboard, sitting, standing, and walking (i.e. out-of-bed). The most important outcome assessed was the modified Rankin scale score after 3 months of stroke. Of these, two studies had positive effects on improving functional capacity. However, evidence on the benefit of early mobilization after 24 h of stroke was the most robust.<sup>7</sup>

In four studies,<sup>17,26,27,29</sup> most patients did not experience any serious adverse events within the first 3 months after stroke. The proportion of patients

**Table 3.** Risk of bias classification.

Risk of bias	High Risk	Low Risk	Uncertain Risk
Random sequence generation	None	Bernhardt, 2015 Bernhardt, 2016 Chippala, 2016 Cumming, 2018 Herisson, 2016 Langhorne, 2017 Polleto, 2015	None
Allocation concealment	None	Bernhardt, 2015 Bernhardt, 2016 Chippala, 2016 Cumming, 2018 Herisson, 2016 Langhorne, 2017 Polleto, 2015	None
Blinding of the participants	Bernhardt, 2015 Bernhardt, 2016 Chippala, 2016 Cumming, 2018 Herisson, 2016 Langhorne, 2017 Polleto, 2015	None	None
Blinding of the outcome assessment	Herisson, 2016	Bernhardt, 2015 Bernhardt, 2016 Chippala, 2016 Cumming, 2018 Langhorne, 2017 Polleto, 2015	None
Incomplete outcome data	Chippala, 2016 Polleto, 2015	Bernhardt, 2015 Bernhardt, 2016 Cumming, 2018 Herisson, 2016 Langhorne, 2017	None
Selective outcome reporting	None	None	Bernhardt, 2015 Bernhardt, 2016 Chippala, 2016 Cumming, 2018 Herisson, 2016 Langhorne, 2017 Polleto, 2015

who experienced non-fatal serious adverse events did not differ significantly between groups (early mobilization compared to usual care). Two studies<sup>28,31</sup> observed no adverse events associated during early mobilization. Only one study<sup>30</sup> observed that one patient had worsening of the neurological status during early sitting, but no changes in vital signs.

### **Risk of bias across studies**

All studies obtained the lowest risk of bias for random sequence generation and allocation concealment and scored high risk in blinding participants. Only Herisson et al. (2016)<sup>30</sup> showed a high risk of blinding of the outcome assessment, and Chippala and Sharma (2016)<sup>28</sup> and Polleto et al. (2015)<sup>31</sup> showed incomplete outcome data (Table 3).

From the included studies and the main outcomes and results, a hospital protocol for early mobilization during the acute phase of stroke was developed (Supplemental file 1). A mobilization ruler was developed for the stroke team to improve care and optimize early mobilization, as well as to guide patients and their families during stroke-unit hospitalization (Supplemental file 2). The ruler can be placed on the patient's bed according to the flowchart shown in Supplemental File 1.

### **Discussion**

This review shows the importance of early mobilization in patients after 24 hours of stroke, in addition, it shows which safety criteria and measurement tools should be used to monitoring



clinical evolution during early mobilization, and the type and frequency of intervention to improve functional outcome after stroke.

### ***When to start the mobilization of the acute patient?***

Attempts have been made to establish the optimal time to start mobilizing patients with acute disease; however, there is still no consensus on this. Smaller studies have shown the benefits of mobilization after 24 h of ictus. Chippala and Sharma<sup>28</sup> assessed the effectiveness of mobilization 18 hours post-ictus and found it beneficial for the recovery of patient functionality. Poletto et al.<sup>31</sup> carried out mobilization during the first 48 h and concluded that it was safe and viable.

Other studies have found no statistical difference between the outcomes of mobilization during the first 24 hours of ictus and conventional physical therapy after 24 hours. Cumming et al.<sup>29</sup> evaluated the response of acute mobilization in relation to the level of cognition and found no significant benefit in the control group. Herisson et al.<sup>30</sup> aimed to seat the patient out of bed as quickly as possible and showed no marked benefit or harm.

The largest study in the literature was the very early rehabilitation trial (AVERT), which was divided into three phases: phase I, a randomized clinical trial; phase II, safety and feasibility studies; and phase III, international and multicentric studies. This study showed that the intervention group in which mobilization was initiated within 24 hours of ictus with higher levels of activities outside the bed had reduced chances of favorable outcomes within the first three months compared with the control group.

These unfavorable effects can be explained by cerebral blood flow. Stroke patients have impaired brain flow self-regulation or vasomotor hyperreactivity, especially in the affected hemisphere. Therefore, they depend directly on systemic blood pressure for good perfusion within the penumbra tissue. It is hypothesized that upright positions may decrease cerebral flow within the first 24 h, which can lead to cerebral penumbra damage (Figure 2).<sup>32,33</sup>

### ***Security criteria for early mobilization***

Before early mobilization during the acute phase of stroke, it is necessary to pay attention to the safety signs that interrupt the exercises. Systolic pressure should be approximately 110–220 mmHg, oxygen saturation should be  $\geq 92\%$  even if  $O_2$  support is required, heart rate should be approximately 40–110 bpm, and temperature should be  $< 38.5^\circ\text{C}$ .<sup>17</sup> In addition, hemodynamic stability should be assessed (there should be no high doses of vasoactive and/or anti-hypertensive drugs) and the level of consciousness should be maintained at a certain level (capable of obeying at least one command indicated by the therapist). The hemoglobin level should be greater than 7 g/dl, and the platelet count should be greater than 50,000.<sup>34</sup> If the patient presents with sweating or other complaints such as excessive tiredness, nausea, headache, and/or nystagmus, mobilization should be suspended, and the patient should be reevaluated. All studies in this review followed the safety recommendations for early mobilization after stroke, and overall, no serious adverse effects were associated with this therapy.

### ***Type and frequency of therapeutic techniques***

Most of the studies showed approaches that prioritize the removal of the patient from the bed as early as possible, and few associated it with another concept or technique.<sup>27,30–35</sup> Only two studies addressed other techniques, including electrostimulation<sup>35</sup> and the Bobath Concept.<sup>31</sup> Yen et al.<sup>35</sup> performed neuromuscular electrostimulation in the lower limbs associated with early mobilization, and they reported that the association between these two techniques improved postural stability and gait in patients with acute stroke within two weeks. Poletto et al.<sup>31</sup> used the Bobath concept for functional training and motor relearning as an early approach within 48 h post-stroke and showed that the technique is safe and feasible.

As there is no consensus on the best technique employed, there is no consensus on the dose and duration of therapy. AVERT demonstrated that shorter durations and higher frequencies compared with usual care were safer, more viable, and more favorable. Although a consensus has not been reached, most studies recommend between 15 and

45 minutes per session, divided into one, two, or three times a day.<sup>27,30–35</sup> However, as mentioned earlier, Donnan et al.<sup>36</sup> started a multicentric study to investigate this more effectively by analyzing the frequency, duration, intensity, and type of therapy with better efficiency.

### **Measurement tools and criteria used to start early mobilization programs**

Most studies use the National Institute of Health Stroke Scale (NIHSS) to measure the severity of stroke. It is a scale with high reliability and easy applicability, but with interobserver variations.<sup>37–39</sup> To monitor the evolution of the patient and the degree of dependence, the Modified Rankin Scale (mRS) with six levels of function was used, with 0 indicating no limitation and 6 indicating death.<sup>40,41</sup> The mRS scale was created not only for the progress of patients but also for quantifying their functionality before the stroke.<sup>42</sup> Another scale widely used during acute stroke studies to assess activities of daily living (ADLs) based on 10 levels of activity (feeding, bathing, routine activities, dressing, intestinal system, urinary system, use of bathroom, transfer, mobility on flat surfaces, stairs) is the Barthel Index; it has scores ranging from 0 to 100, and higher scores are associated with greater independence in performing ADLs.<sup>43</sup>

The three scales presented above have already been validated in Brazil, and their high reliability has been verified.<sup>44</sup> Of the studies selected in this review, all used the NIHSS for determining stroke severity and mRS for monitoring patient progress, except the study by Yen et al. 2019<sup>35</sup>, who did not use mRS for long-term follow-up. The Barthel index is widely used as the main scale to assess activities of daily living.

The patient was removed from the bed based on the outcomes of the assessment using the mRS scale (mRS < 2). However, no study has established the best physical therapy for patients with an mRS greater than 3.<sup>17,27,30</sup> It is known that higher NIHSS scores and lower Barthel indexes are associated with greater degrees of dependence and involvement of patients, but no study found in this review used them as a cutoff point or to define a technique for mobilization. However, in the

AVERT study, it was observed that individuals with NIHSS scores above 16 had worse functional outcomes when mobilized early out of bed.<sup>17</sup>

### **Limitations and clinical applicability**

The included studies had some limitations. No Delphi systematization was used to guide the rehabilitation protocol in this review. In addition, the included studies did not fully consider individual functionality according to the International Classification of Functionality, Disability, and Health (ICF) concept. Individual functionality has a dynamic interaction with health conditions, environmental factors, and personal factors, which can impact long-term outcomes. Therefore, some health domains should focus on body functions and structures, activity and participation, environmental factors, and personal factors.<sup>45</sup>

All evaluated studies considered only the function and structure domain (disability), and no instruments were used to measure activity, participation, and personal and environmental factors. Therefore, the beneficial impact of early mobilization on these other domains and the response to these other items with a positive impact on structure and function has not been established. Limitations and restrictions in activities and participation may indeed be most relevant to patients with stroke. The areas that are covered represent key issues for patients with stroke, including mobility, self-care, communication, and learning.<sup>46</sup> Furthermore, contextual factors like health services (e.g. stroke unit care and rehabilitation interventions) can facilitate the implementation of early mobilization and improve stroke functional outcome in long-term.<sup>46</sup>

Thus, with the systematic review, it was shown that it is possible to create a physiotherapeutic care protocol (Supplemental file 1), with practical guides for family members, and a mobilization ruler for health professionals (Supplemental File 2).

### **Conclusion**

Based on qualitative synthesis, the optimal time to start early mobilization is > 24 h of stroke according to hemodynamic stability and safety criteria. The

duration of mobilization is recommended between 15 and 45 minutes per session, divided into one, two, or three times a day. The early mobilization is safe, and the focus should be on sitting, standing, and walking (i.e. out-of-bed) activity.

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