

ORIGINAL RESEARCH



Title- Effect of early mobilization in mild and moderate intracerebral bleed patients.

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Abstract

Background. Intracranial hemorrhage (ICH) is a critical and often life-threatening condition characterized by bleeding within the intracranial vault, including the brain parenchyma and surrounding meningeal spaces. Early mobilization was defined as early out-of-bed activities of daily living (ADLs), based on the concepts of very early mobilization in stroke patients³ and associated enhanced functional outcomes. Few studies have addressed early out-of-bed mobilization specifically in acute intracerebral hemorrhage (ICH) patients. Patient benefit in such cases is unclear, with early intervention timing and duration identical to those in standard care.

Aims and Objective. This is a prospective, observational, single center study done in Department of neurology GSVM medical college hospital Kanpur in 60 patients of mild to moderate intracerebral bleed patients: 1st March.2022 to 1st March 2024. The main aim of this study is 'Effect of early mobilization in mild and moderate intracerebral bleed patients. We investigated the efficacy of an early mobilization (EM) protocol, administered within 24 to 72 hours of stroke onset, for early functional independence in mild-moderate ICH patients.

Methods. In this study Sixty patients admitted to a stroke center within 24 hours of ICH were randomly assigned to early mobilization (EM) or standard early rehabilitation (SER). The EM group underwent an early out-of-bed mobilization protocol, while the SER group underwent a standard protocol focusing on in-bed training in the stroke center. Intervention in both groups lasted 30 minutes per session, once a day, 5 days a week. Motor subscales of the Functional Independence Measure (FIM-motor), Postural Assessment Scale for Stroke Patients, and Functional Ambulation Category (FAC) were evaluated (assessor-blinded) at baseline, and at 2 weeks, 4 weeks, and 3 months after stroke. Length of stay in the stroke center was also recorded.



Results. mean time to first mobilization after symptom onset was 51.60 hours in the EM group and 135.02 hours in the SER group ($P < .001$). At baseline, the 2 groups were similar regarding age, height, weight, gender, hematoma volume, stroke site, lesion location, initial NIHSS score, NIHSS upper-extremity and lower-extremity subscale scores, ICH score at admission, initial FIM-motor score, PASS score, and FAC level. In addition, the median number of treatment sessions per group during the acute phase was similar: EM 7.0 (range 2-18) versus SER 6.5 (range 2-19) ($P = .988$ between groups). The EM group showed significant improvement in FIM-motor score at all evaluated time points ($P = .004$) and in FAC outcomes at 2 weeks ($P = .033$) and 4 weeks ($P = .011$) after stroke. Length of stay in the stroke center was significantly shorter for the EM group ($P = .004$).

Conclusion- early mobilization in a stroke center within 24 to 72 hours of stroke onset, specifically in patients with mild or mild-moderate ICH, and using an EM protocol with standard intervention time and session frequency, may be more effective than standard early rehabilitation in achieving functional independence within 3 months of stroke.

Keywords- early mobilization, standard early rehabilitation, intracerebral hemorrhage.

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Introduction-

Intracranial hemorrhage (ICH) is a critical and often life-threatening condition characterized by bleeding within the intracranial vault, including the brain parenchyma and surrounding meningeal spaces. Intracranial hemorrhage is defined as any bleeding within the intracranial vault. The mortality rate is extremely high, reaching approximately 50% within the first month and for those who survive, there is a notable risk of severe disability. In an intensive care unit (ICU), early mobilization, implementing mobility within 72 hours of ICU admission, is used with the intention of maintaining or restoring musculoskeletal strength and function, and potentially improving overall functionality.^{1,2} Recently, early mobilization was defined as early out-of-bed activities of daily living (ADLs), based on the concepts of very early mobilization in stroke patients³ and associated enhanced functional outcomes.⁴ Very early mobilization with higher-frequency sessions in an out-of-bed mobility-based training protocol within 24 hours of stroke onset may be associated with a worse outcome at 3 months poststroke,^{7,8} but most studies examine the beneficial effects of early mobilization commencing within 24 to 72 hours of stroke.^{4,9-12} However, early mobilization within 24 to 72 hours might also worsen any poststroke hypertension and increase the risk of

rebleeding, resulting in early deterioration after acute intracerebral hemorrhage (ICH).¹³

ICH is associated with a different pathophysiology and acute management strategy than cerebral infarction, and it is possible that early mobilization may have different effects in patients with ICH rather than ischemia. However, there have been relatively few findings in stroke intervention trials of early mobilization involving participants with hemorrhagic stroke.^{16,17}

Among

ADL measures for stroke patients, the Functional Independence Measure (FIM) is a widely used functional performance instrument developed specifically for inpatient acute rehabilitation.³³ The aim of this randomized, controlled study was to investigate if an early out-of-bed mobilization

protocol started within 24 to 72 hours of stroke onset (compared with an early standard rehabilitation protocol), and with intervention time and daily session duration similar to those in standard care, would lead to improvements in functional independence measures during the early period in patients with acute ICH.

Methods-

This is a prospective, observational, single center study done in Department of neurology GSVM medical college hospital Kanpur in 60 patients of mild to moderate intracerebral bleed patients: 1st March.2022 to 1st March 2024. The main aim of this study is 'Effect of

early mobilization in mild and moderate intracerebral bleed patients. We investigated the efficacy of an early mobilization (EM) protocol, administered within 24 to 72 hours of stroke onset, for early functional independence in mild to moderate ICH patients.

ICH stroke patients admitted to the stroke center were screened and consecutively enrolled after meeting the eligibility criteria for intensive antihypertensive treatment (primarily intravenous nicardipine infusion). The study was approved by the institutional review board. Written informed consent was obtained from all participants before randomization.

All research procedures were conducted in accordance with ethical standards of the Declaration of Helsinki. The primary endpoint was total score on the motor sub-scale of the FIM (FIM-motor) assessed 3 months after stroke.

Study sample size calculations were based on a low estimate of 17 points for minimum clinically important difference (MCID) in FIM-motor assessment between the 2 groups at all follow-up points. Twenty-seven subjects per group would be required, assuming a standard deviation of approximately 30% in a 2-tailed test, with a α level of 0.05 and a power level of 80%. A total of 60 patients were included to allow for a dropout rate of approximately 10%.

Patients presented to the stroke center at NTUH \leq 24 hours after ICH were considered for the study.

Inclusion criteria were: a first-time primary ICH with unilateral hemiparesis/hemiplegia confirmed via computed tomography; no contraindications to mobilization (early intervention) within 72 hours of stroke onset (based on the medical team's clinical judgment, systolic blood pressure (SBP) $<$ 160 mm Hg at rest, resting heart rate $<$ 130 bpm, oxygen saturation $>$ 92% without supplementation, and no hydrocephalus before intervention and age 20 to 80 years.³⁹⁻⁴¹

Exclusion criteria were secondary ICH due to trauma, surgery, hemorrhagic transformation from stroke, or an underlying mass; living alone and unable to complete the baseline survey because of serious aphasia, language difficulties, or cognitive deficit; other medical conditions, including severe heart failure, acute

coronary syndrome, active gastrointestinal blood loss, or lower-limb disorders, preventing early mobilization; and an inability to provide informed consent or previous enrollment in another intervention trial. In addition, we excluded patients with rapidly deteriorating symptoms within 24 hours of stroke, those who underwent immediate surgery; and those with a concurrent diagnosis of rapidly deteriorating disease (eg, terminal cancer).

Study participants were randomized into 1 of 2 groups and underwent different rehabilitation protocols: early mobilization within 24 to 72 hours of stroke onset (EM group); or standard early rehabilitation (SER group).

After randomization, a baseline assessment of demographic and disease characteristics, and medical history were conducted for each participant. Outcome measures were collected at baseline (preintervention), and at 2 weeks, 4 weeks, and 3 months after stroke onset. Secondary outcomes included the Postural Assessment Scale for Stroke Patients (PASS),⁵¹ the Functional Ambulation Category (FAC),⁵² and the mean duration of stay in the stroke center. The duration of stay in the stroke center was defined as the time from admission to being declared medically fit for discharge by the senior ICU clinician.

All adverse events, including neurologic deterioration, hypotension, falls, and line dislodgements, during the intervention period were recorded.

Statistical analysis- Results were analyzed using Statistical Package for the Social Sciences version 22.0 (IBM SPSS Statistics, Armonk, NY, USA). We assessed all patients who underwent at least 1 treatment session (intention-to-treat principle), and intent-to-treat analyses were used for all outcome comparisons. Descriptive statistics were expressed as mean (standard deviation, SD) for continuous variables, and as median (interquartile range, IQR) for ordinal variables. Number (n) and percent (%) were used for categorical variables. All continuous variables were first assessed for normality using the Shapiro-Wilk test and transformed when necessary to meet the assumption of normal distribution. Desc

riptive statistics were used to define relevant patient characteristics.

For total FIM-motor and PASS scores, we explored the associations between potential factors and outcomes of interest using a linear mixed model. The Mann-Whitney *U* test was used to identify any significant differences in FAC measurements between the 2 groups. The independent-sample *t* test was used to identify any significant differences in mean duration of stay in the stroke center. All hypothesis tests used a significance level of $P < .05$.

Results-

Sixty patients were randomized into 2 groups, with equal numbers ($n = 30$) in each group. After 3 months' follow-up, there were 2 dropouts in each group due to family reasons, but all patients were included in the final analysis. Participant characteristics at study enrollment are shown in Table 1, which were equivalent in the 2 groups except for 1 outcome measure: mean time to first mobilization after symptom onset was 51.60 hours (SD 14.15) in the EM group and 135.02 hours (SD 33.05) in the SER group ($P < .001$). At baseline, the 2 groups were similar regarding age, height, weight, gender, hematoma volume, stroke site, lesion location,

initial NIHSS score, NIHSS upper-extremity and lower-extremity subscale scores, ICH score at admission, initial FIM-motor score, PASS score, and FAC level. In addition, the median number of treatment sessions per group during the acute phase was similar: EM 7.0 (range 2-18) versus SER 6.5 (range 2-19) ($P = .988$ between groups). None of the participants in either group experienced adverse effects, including neurologic deterioration, hypotension, falls, or line dislodgements, during early rehabilitation or mobilization.

Table 2 shows total FIM-motor score, FIM-motor self-care tasks subscale score, FIM-motor transfers plus locomotion subscale score, and total PASS score in the 2 groups at baseline, and at 2 weeks, 4 weeks, and 3 months after stroke. In the preliminary regression analysis for total FIM-motor scores, including group, time, and the group \times time interaction term as fixed effects, and baseline FIM-motor scores as a random effect, no statistically significant difference was found in the interaction term ($F = 0.004, P = .949$). Similar results were noted for the FIM-motor self-care tasks subscale ($F = 0.231, P = .631$), for the FIM-motor transfers plus locomotion subscales ($F = 0.016, P = .901$), and for PASS score ($F = 0.235, P = .628$). Thus, subsequent analysis did not include the interaction term in the model.

Table 1. Participant Characteristics.			
Group	SER (n=30)	EM (n=30)	P
Age (years), mean \pm SD	59.33 \pm 13.13	58.77 \pm 11.68	.860 ^a
Height (cm), mean \pm SD	165.00 \pm 9.34	164.73 \pm 8.31	.907 ^a
Weight (kg), mean \pm SD	68.67 \pm 17.45	71.01 \pm 17.41	.606 ^a
Gender (female/male), n	8:22	9:21	.774 ^b
Lesion site (right/left), n	11:19	14:15	.400 ^b
The ICH score (0/1)	26:4	24:6	.488 ^b
ICH location (supratentorial/infratentorial), n	27:	27:3	1.000 ^b

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ICH volume (mL), mean ± SD	10.03 ± 6.33	6.65 ± 7.95	.073 ^a
Time to first physical therapy intervention (hours), mean ± SD	47.70 ± 16.77	41.80 ± 17.07	.182 ^a
Time to first mobilization (hours), mean ± SD	135.02 ± 33.05	51.60 ± 14.15	<.001* ^a
NIHSS total scores at admission, median (range)	6.5 (2-15)	5 (2-20)	.165 ^c
NIHSS scores at upper extremities sub scores, median (range)	2 (0-4)	1 (0-4)	.173 ^c
NIHSS scores at lower extremities sub scores, median (range)	2 (0-4)	1 (0-4)	.178 ^c
Initial PASS scores, mean ± SD	5.37 ± 6.03	7.40 ± 5.05	.162 ^a
Initial FIM-motor scores, mean ± SD	18.90 ± 9.87	18.53 ± 4.82	.856 ^a
Initial FAC level, median (IQR)	0 (0-0)	0 (0-0)	.161 ^d

Abbreviations: SER, standard early rehabilitation; EM, early mobilization; ICH, intracerebral hemorrhage; ICH scores, The Intracerebral Hemorrhage Score; NIHSS, National Institute of Health Stroke Scale; PASS, Postural Assessment Scale for Stroke patients; FIM-motor: motor subscales of the Functional Independence Measure; FAC, Functional Ambulation Category; IQR, interquartile range.

Table 2. The Level of the FAC Measure at Each Follow-up Assessment in Both Groups.

Variables	Time	Group		P (Group Effect)
		SER (n=30)	EM (n=30)	
FAC	2 weeks post stroke, median (IQR)	3 (0.75-4)	3 (3-4)	.033*
	4 weeks post stroke, median (IQR)	3 (3-4.25)	5 (3-5)	.011*
	3-month follow-up after stroke, median (IQR)	4 (3-5)	5 (4-5)	.08

Abbreviations: SER, standard early rehabilitation; EM, early mobilization; FAC, Functional Ambulation Category; IQR, interquartile range.

*Significant difference by Mann-Whitney U test ($P < .05$).

We found that group effects were significant at all evaluation times for FIM-motor total score ($F = 8.859$, $P = .004$), FIM-motor self-care tasks subscale score ($F = 8.868$, $P = .005$), and FIM-motor transfers plus locomotion ability subscale score ($F = 4.997$, $P = .029$). However, no significant group effect was seen for the EM versus SER protocol (dose-matched therapy), specifically in acute ICH patients in a stroke center and starting within 24 to 72 hours of stroke onset.

Our results demonstrated that the EM versus SER protocol produced significantly greater FIM-

motor scores, and may accelerate ADL restoration within 3 months of ICH. Patients who underwent the EM rather than SER protocol after ICH also had a shorter duration of stay in the stroke center and reported significantly greater walking independence within 4 weeks of stroke onset. Regarding evidence supporting early mobilization and specific to ICH patients, one previous study showed that ICH patients admitted to neurology wards or rehabilitation units within 48 hours, and who underwent very early rehabilitation, had si-



gnificantly greater ADL independence 6 months after stroke, compared with patients who started rehabilitation >7 days after stroke.²⁷ However, the aim of the current study was to compare the efficacy of early rehabilitation, implemented within 48 hours of stroke, with rehabilitation implemented ≥ 7 days post-stroke, rather than to compare 2 different protocols started at the same time.²⁷ In the prespecified dose-response analysis of AVERT, trends disfavored "early" (time from stroke onset to first out-of-bed mobilization), more intensive rehabilitation group with hemorrhagic stroke when compared with usual care, which resulted in improved functional outcomes.⁵⁴ However, a follow-up analysis suggested that the specific frequency and duration of mobilization sessions needed to be optimized to avoid the harmful effects of aggressive early mobilization.⁵⁴

In other critically ill patients in ICUs, early mobility has been linked to improved functional status.⁵⁷ In the present study, total FIM-motor score and FIM-motor subscale score for self-care tasks highlighted important benefits within 3 months after stroke: That is, an EM protocol started within 24 to 72 hours of stroke onset promoted greater ADL independence in mild-moderate acute ICH patients. Indeed, functional recovery from a stroke event occurs through a combination of spontaneous and experience-dependent processes.²⁰ In our study, active and unsupported sitting out of bed constituted early mobilization, with the opportunity to stand. The EM protocol used in our study may enhance motor experiences or provide greater stimulation than a SER protocol. Moreover, we found early recovery of walking independence in the EM group, for which a similarly significant group difference was evident regarding FIM-motor subscale score for transfers plus locomotion ability at 4 weeks after stroke. This suggests that patients who receive an EM protocol rather than standard care may be more active once transferred to an ordinary ward. Some previous results showed that ambulation distance at ICU discharge was greater in patients who received early active

mobilization in the ICU, compared with patients for whom mobilization was started after ICU discharge.^{58,59} In addition, shorter ICU stays have been reported in adult patients with primary neurologic injury receiving progressive EM therapy.⁶⁰ In the present study, while the EM protocol was implemented to reduce stroke impact, associated reductions in duration of stay in the stroke center were also observed.

Besides the lack of significant differences in postural stability at all evaluation time points, we also found no differences between the 2 groups in FAC-level outcomes at 3 months poststroke. We cannot rule out the possibility that other intensive training at the sub-acute stage might have achieved similar improvements in walking ability. However, the ICH patients in our study had relatively low NIHSS and ICH scores at admission. Lower NIHSS scores indicate fewer neurologic deficits, and a previous study found that paresis severity was a predictor of mobility 30 days after stroke. An ICH score <3 predicts a good outcome at 30 days, which is defined as an mRS score of ≤ 2 .³⁹ Consistent with the above, most participants in the present study had good posture control after the acute phase and had walking recovery at 3 months poststroke; thus, it may have been difficult to detect further progress regarding posture control outcomes because of a ceiling effect. Another probable reason is that the study was underpowered to detect such long-term differences in walking ability; each group was of relatively small size.

Conclusion- early mobilization in a stroke center within 24 to 72 hours of stroke onset, specifically in patients with mild to moderate ICH, and using an EM protocol with standard intervention time and session frequency, may be more effective than standard early rehabilitation in achieving functional independence within 3 months of stroke.

References-

1. Leditschke IA, Green M, Irvine J, Bissett B, Mitchell IA. What are the barriers to mobilizing intensive care patients? *Cardiopulm Phys Ther J*. 2012;23:26-29.
2. Bein T, Bischoff M, Bruckner U, et al. S2e guideline: positioning and early mobilisation in prophylaxis or therapy of pulmonary disorders: revision 2015: S2 guideline of the German Society of Anaesthesiology and Intensive Care Medicine (DGAI). *Anaesthesist*. 2015;64(suppl 1):1-26.
3. Bernhardt J, Indredavik B, Dewey H, et al. Mobilisation "inbed" is not mobilisation. *Cerebrovasc Dis*. 2007;24:157-158.
4. Bernhardt J, Dewey H, Thrift A, Collier J, Donnan G. A Very Early Rehabilitation Trial for stroke (AVERT): phase II safety and feasibility. *Stroke*. 2008;39:390-396.
5. Bernhardt J, Thuy MN, Collier JM, Legg LA. Very early versus delayed mobilisation after stroke. *Cochrane Database Syst Rev*. 2009;(1):CD006187.
6. Chippala P, Sharma R. Effect of very early mobilisation on functional status in patients with acute stroke: a single-blind, randomized controlled trial. *Clin Rehabil*. 2016;30:669-675.
7. AVERT Trial Collaboration Group. Efficacy and safety of very early mobilisation within 24 hours of stroke onset (AVERT): a randomised controlled trial. *Lancet*. 2015;386:46-55.
8. Lynch E, Hillier S, Cadilhac D. When should physical rehabilitation commence after stroke: a systematic review. *Int J Stroke*. 2014;9:468-478.
9. Langhorne P, Stott D, Knight A, Bernhardt J, Barer D, Watkins C. Very early rehabilitation or intensive telemedicine after stroke: a pilot randomised trial. *Cerebrovasc Dis*. 2010;29:352-360.
10. Sundseth A, Thommessen B, Ronning OM. Outcome after mobilization within 24 hours of acute stroke: a randomized controlled trial. *Stroke*. 2012;43:2389-2394.
11. Yelnik AP, Quintaine V, Andriantsifanetra C, et al; AMOBES Group. AMOBES (Active Mobility Very Early After Stroke): a randomized controlled trial. *Stroke*. 2017;48:400-405.
12. Diserens K, Moreira T, Hirt L, et al. Early mobilization out of bed after ischaemic stroke reduces severe complications but not cerebral blood flow: a randomized controlled pilot trial. *Clin Rehabil*. 2012;26:451-459.
13. Manning L, Hirakawa Y, Arima H, et al; INTERACT2 Investigators. Blood pressure variability and outcome after acute intracerebral haemorrhage: a post-hoc analysis of INTERACT2, a randomised controlled trial. *Lancet Neurol*. 2014;13:364-373.
14. Skarin M, Bernhardt J, Sjöholm A, Nilsson M, Linden T. "Better wear out sheets than shoes": a survey of 202 stroke professionals' early mobilisation practices and concerns. *Int J Stroke*. 2011;6:10-15.
15. Ali M, Bath P, Brady M, et al; VISTA Steering Committees. Development, expansion, and use of a stroke clinical trials resource for novel exploratory analyses. *Int J Stroke*. 2012;7:133-138.
16. Bayley MT, Bowen A, English C, Teasell R, Eng JJ. Where to now? AVERT answered an important question, but raised many more. *Int J Stroke*. 2017;12:683-686.
17. Bernhardt J, Raffelt A, Churilov L, et al; AVERT Trialists' Collaboration. Exploring the threat to generalisability in a large international rehabilitation trial (AVERT). *BMJ Open*. 2015;5:e008378.
18. Rothwell PM. AVERT: a major milestone in stroke research. *Lancet*. 2015;386:7-9.
19. Masters L, Barreca S, Ansley B, Waid K, Buckley S. Functional mobility training for individuals admitted to acute care following a stroke: a prospective study. *Top Stroke Rehabil*. 2007;14:1-11.



20. Murphy TH, Corbett D. Plasticity during stroke recovery: from synapse to behaviour. *Nat Rev Neurosci*. 2009;10:861-872.
21. Krakauer JW, Carmichael ST, Corbett D, Wittenberg GF. Getting neurorehabilitation right: what can be learned from animal models? *Neurorehabil Neural Repair*. 2012;26:923-931.
22. Pekna M, Pekny M, Nilsson M. Modulation of neural plasticity as a basis for stroke rehabilitation. *Stroke*. 2012;43:2819-2828.
23. Mestriner RG, Pagnussat AS, Boisserand LS, Valentim L, Netto CA. Skilled reaching training promotes astroglial changes and facilitates sensorimotor recovery after collagenase-induced intracerebral hemorrhage. *Exp Neurol*. 2011;227:53-61.
24. Auriat AM, Wowks S, Colbourne F. Rehabilitation after intracerebral hemorrhage in rats improves recovery with enhanced dendritic complexity but no effect on cell proliferation. *Behav Brain Res*. 2010;214:42-47.
25. Caliaperumal J, Colbourne F. Rehabilitation improves behavioral recovery and lessens cell death without affecting iron, ferritin, transferrin, or inflammation after intracerebral hemorrhage in rats. *Neurorehabil Neural Repair*. 2014;28:395-404.
26. Williamson MR, Dietrich K, Hackett MJ, et al. Rehabilitation augments hematoclearance and attenuates oxidative injury and ion dyshomeostasis after brain hemorrhage. *Stroke*. 2017;48:195-203.
27. Liu N, Cadilhac DA, Andrew NE, et al. Randomized controlled trial of early rehabilitation after intracerebral hemorrhage stroke: difference in outcomes within 6 months of stroke. *Stroke*. 2014;45:3502-3507.
28. Craig LE, Bernhardt J, Langhorne P, Wu O. Early mobilization after stroke: an example of an individual patient data meta-analysis of a complex intervention. *Stroke*. 2010;41:2632-2636.
29. Indredavik B, Bakke F, Slordahl SA, Rokseth R, Haheim LL. Treatment in a combined acute and rehabilitation stroke unit: which aspects are most important? *Stroke*. 1999;30:917-923.
30. Bernhardt J, Godecke E, Johnson L, Langhorne P. Early rehabilitation after stroke. *Curr Opin Neurol*. 2017;30:48-54.
31. Altman DG, Royston P. The cost of dichotomising continuous variables. *BMJ*. 2006;332:1080.
32. Luft AR, Kesselring J. Critique of a Very Early Rehabilitation Trial (AVERT). *Stroke*. 2016;47:291-292.
33. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. *Adv Clin Rehabil*. 1987;1:6-18.
34. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311:507-520.
35. Beninato M, Gill-Body KM, Salles S, Stark PC, Black-Schaffer RM, Stein J. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. *Arch Phys Med Rehabil*. 2006;87:32-39.
36. Wang H, Camicia M, DiVita M, Mix J, Niewczyk P. Early inpatient rehabilitation admission and stroke patient outcomes. *Am J Phys Med Rehabil*. 2015;94:85-96.
37. Imura T, Nagasawa Y, Fukuyama H, Imada N, Oki S, Araki O. Effect of early and intensive rehabilitation in acute stroke patients: retrospective pre/post-comparison in Japanese hospital. *Disabil Rehabil*. 2018;40:1452-1455.



38. Cheung RT, Zou LY. Use of the original, modified, or new intracerebral hemorrhage score to predict mortality and morbidity after intracerebral hemorrhage. *Stroke*. 2003;34:1717-1722.
39. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke*. 2001;32:891-897.
40. Alonso A, Ebert AD, Kern R, Rapp S, Hennerici MG, Fatar M. Outcome predictors of acute stroke patients in need of intensive care treatment. *Cerebrovasc Dis*. 2015;40:10-17.
41. Forti P, Maioli F, Magni E, et al. Risk of exclusion from stroke rehabilitation in the elderly. *Arch Phys Med Rehabil*. 2018;99:477-483.
42. Meyer BC, Lyden PD. The modified National Institutes of Health Stroke Scale: its time has come. *Int J Stroke*. 2009;4:267-273.
43. Bernhardt J, Dewey H, Thrift A, Donnan G. Inactive and alone: physical activity within the first 14 days of acute stroke unit care. *Stroke*. 2004;35:1005-1009.
44. Langhorne P, Pollock A; Stroke Unit Trialists' Collaboration. What are the components of effective stroke unit care? *Age Ageing*. 2002;31:365-371.
45. Herisson F, Godard S, Volteau C, et al; SEVEL Study Group. Early sitting in ischemic stroke patients (SEVEL): a randomized controlled trial. *PLoS One*. 2016;11:e0149466.
46. Gosselink R, Bott J, Johnson M, et al. Physiotherapy for adult patients with critical illness: recommendation of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on physiotherapy for critically ill patients. *Intensive Care Med*. 2008;34:1188-1199.
47. Bernhardt J, English C, Johnson L, Cumming TB. Early mobilization after stroke: early adoption but limited evidence. *Stroke*. 2015;46:1141-1146.
48. Bernhardt J, Chitravas N, Meslo L, Thrift A, G, Indredavik B. Not all stroke units are the same: a comparison of physical activity patterns in Melbourne, Australia, and Trondheim, Norway. *Stroke*. 2008;39:2059-2065.
49. Hu MH, Hsu SS, Yip PK, Jeng JS, Wang YH. Early and intensive rehabilitation predicts good functional outcomes in patients admitted to the stroke intensive care unit. *Disabil Rehabil*. 2010;32:1251-1259.
50. Dodds TA, Martin DP, Stolov WC, Deyo RA. A validation of the functional independence measurement and its performance among rehabilitation inpatients. *Arch Phys Med Rehabil*. 1993;74:531-536.
51. Benaim C, Pérennou DA, Villy J, Rousseaux M, Pelissier JY. Validation of a standardized assessment of postural control in stroke patients: the Postural Assessment Scale for Stroke Patients (PASS). *Stroke*. 1999;30:1862-1868.
52. Holden MK, Gill KM, Magliozzi MR. Gait assessment for neurologically impaired patients. Standards for outcome assessment. *Phys Ther*. 1986;66:1530-1539.
53. Perry J, Garrett M, Gronley JK, Mulroy SJ. Classification of walking handicap in the stroke population. *Stroke*. 1995;26:982-989.
54. Bernhardt J, Churilov L, Ellery F, et al. Prespecified dose-response analysis for a Very Early Rehabilitation Trial (AVERT). *Neurology*. 2016;86:2138-2145.
55. Bahouth MN, Power MC, Zink EK, et al. Safety and feasibility of a neuroscience critical care program to mobilize patients with primary intracerebral hemorrhage. *Arch Phys Med Rehabil*. 2018;99:1220-

- 1225.
56. Rand ML, Darbinian JA. Effect of a evidence-based mobility intervention on the level of function in acute intracerebral and subarachnoid hemorrhagic stroke patients on a neurointensive care unit. *Arch Phys Med Rehabil.* 2015;96:1191-1199.
57. Fuest K, Schaller SJ. Recent evidence on early mobilization in critical-ill patients. *Curr Opin Anaesthesiol.* 2018;31:144-150.
58. Clark DE, Lowman JD, Griffin RL, Matthews HM, Reiff DA. Effectiveness of an early mobilization protocol in a trauma and burns intensive care unit: a retrospective cohort study. *Phys Ther.* 2013;93:186-196.
59. Bailey P, Thomsen GE, Spuhler VJ, et al. Early activity is feasible and safe in respiratory failure patients. *Crit Care Med.* 2007;35:139-145.
60. Klein K, Mulkey M, Bena JF, Albert NM. Clinical and psychological effects of early mobilization in patient treated in a neurologic ICU: a comparative study. *Crit Care Med.* 2015;43:865-873.