Efficacy of Early Initiation of Rehabilitation on Motor Function and Functional Recovery of Patients with Acute Intracerebral Hemorrhage: A Meta-Analysis

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ABSTRACT

Background
Acute ICH represents a serious form of stroke, associated with high morbidity and mortality. Early rehabilitation has been recommended in order to improve motor function recovery and functional independence of the patients with ICH. However, the timing at which rehabilitation should be initiated remains unclear.

Objectives
This study aims to determine the effectiveness of early rehabilitation in motor function recovery and functional independence as well as to investigate the ideal timing for initiating rehabilitation post-ICH.

Methods
Four RCTs were retrieved in this meta-analysis (Bai et al – 364 patients, Liu et al – 243 patients, Yen et al – 60 patients, Zhu et al – 84 patients). Selection criteria included early rehabilitation intervention for acute ICH patients, with measurable objective assessment of motor function and evaluation of ADLs at 1 and 3 months post-rehabilitation. Data extraction was done from the selected studies, followed by statistical analysis, using a random effects model, calculating the SMD with 95% CI.

Results
Early rehabilitation significantly improved motor function at 1 month [SMD = 0.55, 95% CI 0.09, 1.00, p = 0.02] and independence in ADLs at 1 month [SMD = 0.57, 95% CI 0.10, 1.05, p = 0.02]. However, this did not persist at 3 months [SMD = 0.17, 95% CI 0.00, 0.35, p = 0.05].

Conclusion
Results of this meta-analysis support that early rehabilitation within 72 hours post-ICH significantly improved motor recovery and independence in ADLs at 1 month but uncertainties still surround benefits at 3 months.

INTRODUCTION
Background

Spontaneous intracerebral hemorrhage is one of the most serious forms of stroke, with a case-fatality rate reaching nearly 40% in the first month. The poor long-term prognosis makes it one of the leading factors for morbidity and mortality worldwide. An addition to these is a systematic review and meta-analysis by Van Asch et al., stating that generally, there is a higher incidence of intracerebral hemorrhage in men than in women; in the Japanese studies; two times higher rate of intracerebral hemorrhage incidence in Asian people compared to other ethnic groups; and an increasing incidence of intracerebral hemorrhage with increasing age.[1]

Research has revealed that early rehabilitation of an individual survivor of ICH may result in better motor recovery, both in the long and shorter terms, and less functional and neurological impairment with an improvement of quality in life. [2, 3, 4, 5]

Although satisfactory, results for early rehabilitation in ICH are promising. The ideal moment to start rehabilitation is still debated among specialists; the guidelines indicate that immediately after an intracerebral hemorrhage, patients must be well monitored, with special reference to the monitoring of blood pressure, a finding that contributes to a more cautious approach in starting rehabilitation.[6]

A randomized controlled trial on early mobilization and its effects on the short-term variability of blood pressure in acute intracerebral hemorrhage patients compared the systolic blood pressure and blood pressure variance between patients who had mobilization early, within 24-72 hours, and those with mobilization later (>72 hours). It concluded that for mild-moderate ICH patients in the acute phase, an early mobilization protocol within 24 to 72 hours of onset is safe to implement. [7]

Although some clinical trials and anecdotal evidence pointed out potential benefits and safety, results are not always consistent. In some studies, improvements in functional recovery ranged from substantial to no significant difference when compared with delayed rehabilitation.

Intervening variations between study design, patient populations, kinds of rehabilitation interventions, and outcome measures pose problems regarding sense-making across such results.[8]

Up to the present, a great deal of research has been carried out to determine the efficacy of early rehabilitation which is defined as initiation of rehabilitation within 72 hours post-ictus after acute cerebrovascular infarction,9,10,11 and data in support of early initiation of rehabilitation after acute ICH still remains insufficient. Due to a lack of standardized guidelines or research to support the early initiation of rehabilitation, variations among medical practitioners persist in relation to the timeline of initiation of rehabilitation post-acute intracerebral hemorrhage.

This meta-analysis will primarily focus on confirming consensus on the best time to initiate rehabilitation following an acute intracerebral hemorrhage.

METHODOLOGY

A review of available literature was done through PubMED, Google Scholar, and PsycNET. Journals up to August 15, 2024 were included. Search was done with the following keywords: (Early Rehabilitation) AND (Acute Intracerebral Hemorrhage) OR (Acute ICH) OR (Early hemorrhagic stroke) AND (Motor function) OR (Functional independence) OR (ADL). The studies were evaluated using predetermined inclusion and exclusion criteria. Inclusion criteria used were: subjects with Acute ICH, use of Early rehabilitation defined as initiation of rehabilitation within 24-72 of stroke onset, outcome of functionality measured objectively with a scale Exclusion criteria used were: patients with major significant co-morbidities or poor prognosis attributed to another condition. Only randomized control studies were used and other study designs were excluded. Duplicate studies were excluded as well. One author and an independent reviewer [B.G.] performed screening of the studies for inclusion according to the predetermined criteria.

Database search (Figure 1) yielded a total of 1429 result. Upon screening of the title and abstracts, 1421 studies were excluded due to not being relevant resulting to 6 studies that initially met the eligibility criteria after screening of title, abstract, and methodology. 2 more studies were excluded due to: 1. Study population not being eligible, and 2. having outcome that is not eligible. A final roster of 4 studies which were then subjected to screening of full available text. All of the 4 studies were included for the meta-analysis.

Statistical Analysis

Data extraction was done from articles with reported outcomes on the efficacy of early initiation of rehabilitation therapy. Data reported in figures was extracted via online digitizer software.

Summary statistics in the form of means and standard deviations of outcome scores were tabulated in Microsoft Excel. Transformations to the data in preparation for meta-analyses were performed using procedures outlined in Chapter 6 of the Cochrane Handbook for Systematic Review of Interventions (Higgins et al., 2023). Values presented as median and interquartile range were transformed into mean and standard deviation following the methodology of McGrath et al. (2020) using the quantile estimation method. Missing standard deviations in the article of Bai et al. (2012) were computed using p-values corresponding to the comparisons between treatment and control groups for each outcome and for every follow up interval.

Analyses were conducted using a random effects model and a generic inverse variance approach. Multiple instruments were used to evaluate the study outcomes; thus, all effect measures were calculated as standardized mean differences with point estimates, 95% confidence intervals and p values. Sensitivity analyses were also conducted via comparisons of effect measures obtained with and without the imputed values of Bai et al. (2012). Heterogeneity was estimated using Chi square and Higgin's I2 statistic, with values classified as minimal, moderate, substantial and considerable for scores of 0-40%, 30-60%, 50-90%, and 75-100% respectively as patterned from the values used in the Cochrane Handbook. Statistical significance = was tagged at p = 0.05. Computations of effect measures and creation of forest plots were done using Cochrane Review Manager (RevMan) 5.4. [12,13]

RESULTS

Four articles were found to have fulfilled the criteria for inclusion in the present study. Table 1 summarizes the articles that were included in this study.

Outcomes with sufficient data for analysis included measures of motor function or recovery after stroke at 1 month after initiation of treatment, and measures of activities of daily living (ADLs) at 1 month and at 3 months post-initiation. Motor function was measured via the Fugl-Meyer Assessment Scale (FMA) and Functional Ambulation Category (FAC). ADL was measured via the Modified Barthel Index (MBI), Barthel Index and the Functional Independence Measure (FIM-motor).

Motor function, represented in Figure 2, was measured and exhibited superiority in the early rehabilitation group compared to controls with an SMD of 0.55 (95% CI 0.09, 1.00, p = 0.02), which is equivalent to a moderately strong effect. Larger magnitudes of this effect were noticed in studies conducted by Yen et al. (2019) and Zhu et al. (2023). The exclusion of Bai et al 2012 dramatically changed the overall effect size toward a much strong effect: SMD = 0.79, 95% CI 0.45, 1.13, p < 0.00001.

Activities of daily living were also found to have had better improvement in the early rehabilitation group (Figure 3). However, this effect was present only at 1 month, SMD = 0.57, 95% CI 0.10, 1.05, p = 0.02, and was no longer significant at 3 months, SMD = 0.17, 95% CI 0.00, 0.35, p =0.05. As seen in the motor function analysis, sensitivity analysis by excluding Bai et al. 2012 yielded a better effect measure in the forest plot at 1 month: SMD = 0.82, 95% CI 0.48, 1.16, p <0.00001. When the same was applied to the analysis at 3 months, very little change was observed.

Table 1. Summary of RCTs included in the study

Aspect	Bai et al. (2011)	Liu et al. (2014)	Yen et al. (2019)	Zhu et al. (2023)
Population	Ictus within 24 hours to 1 week; GCS > 8; limb disability	Ictus within 48 hours; first ICH	First-time ICH, hemiparesis/ hemiplegia, within 72 hours	Post-operative brainstem hemorrhage patients
Age Range	40-80 years old	58.5 (12.3)/ 59.1 (15.5)	20-80 years old	50-75 years old
Exclusion Criteria	Chronic CVD, tetraplegia, dementia	Severe motor impairments, heart failure, language or cognitive deficits	Rapid symptom deterioration, severe heart failure, language deficits	Trauma, mental illness, hearing/cognitive disorders, deep coma, malignant tumors
Rehabilitation Initiation	Within 24 hours of admission	Within 48 hours of ICH onset	Within 24-72 hours of ICH onset	Early rehabilitation post-surgery
Control Group	Delayed initiation of rehabilitation	Rehabilitation after 7 days	Rehabilitation after ICU discharge	Conventional Western medicine only
Treatment Modalities	3-step rehabilitation (ADLs, balance, motor function improvement)	ADL exercises, neuromuscular stimulation, task-specific practice	Out-of-bed mobilization (sitting, standing, stepping)	Neurological and motor function training
Frequency	45 min/day, 5x/week	≥16× per month, 60 min/session	5 days/week, 30 min/ session	30 min/session, 5x/week, for 4 weeks
Outcome Measures	FMA, MBI	Barthel Index	FIM, FAC	FMA, Barthel Index
Motor Function Results	FMA significantly higher in the rehabilitation group at 1 and 3 months	Statistically significant improvement in Barthel Index at 3 months in intervention group	Significant improvements in FIM motor score and independent walking at 4 weeks (P = .011)	FMA significantly higher in the rehabilitation group (P < 0.05)
Functional Independence Results	MBI significantly higher in rehabilitation group	Improvement in Barthel Index after 3 months	FAC showed significant improvement in walking ability at 4 weeks but not at 3 months	Barthel Index significantly improved in the rehabilitation group

Figure 2. Forest plot of post-stroke motor function/recovery in early rehabilitation vs control groups measured 1 month following initiation of treatment

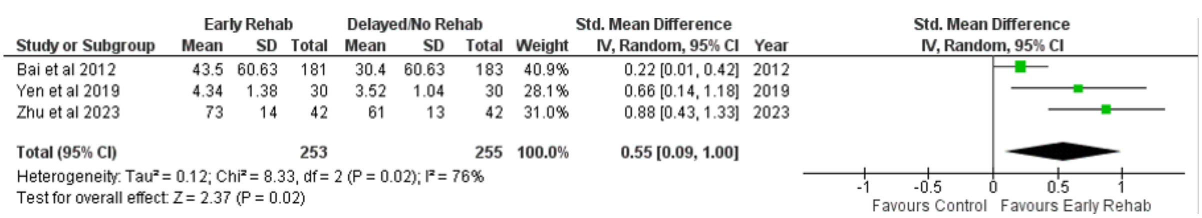
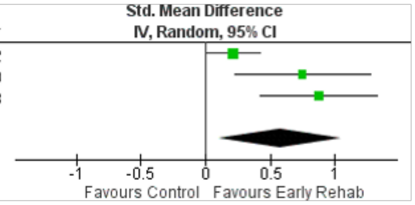


Figure 3. Forest plot of post-stroke activities of daily living in early rehabilitation vs control groups measured (A) 1 month and (B) 3 months following initiation of treatment.

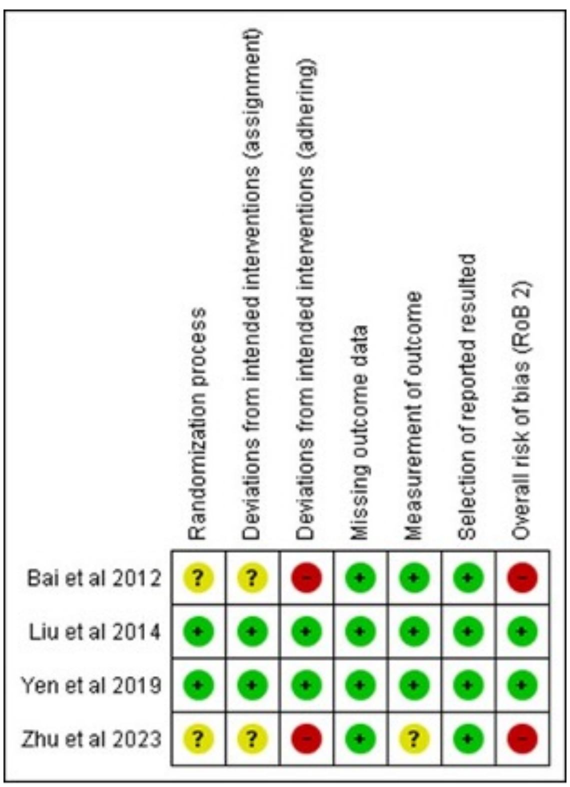
Study or Subgroup	Early Rehab Mean	Early Rehab SD	Early Rehab Total	Delayed/No Rehab Mean	Delayed/No Rehab SD	Delayed/No Rehab Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Bai et al 2012	42	37.95	181	33.8	37.95	183	40.3%	0.22 [0.01, 0.42]	2012
Yen et al 2019	82.4	14.85	30	68.33	21.65	30	28.4%	0.75 [0.22, 1.27]	2019
Zhu et al 2023	75	15	42	63	12	42	31.3%	0.88 [0.43, 1.32]	2023
Total (95% CI)			**253**			**255**	**100.0%**	**0.57 [0.10, 1.05]**	

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 9.02$, df = 2 (P = 0.01); $I^2 = 78\%$
Test for overall effect: Z = 2.38 (P = 0.02)



There was considerable heterogeneity for analysis of both motor function, I2 = 76%, p = 0.02, and ADLs, I2 = 78%, p = 0.01, at 1 month. At 3 months, analysis of ADLs resulted in relatively homogenous results, I2 = 14%, p = 0.31. Risk of bias assessment of included articles are shown in Figure 4. The studies by Liu et al. (2014), and Yen et al. (2019) were well documented with regards to study procedures right from the randomization of participants up to recording of outcomes and had few issues as it regarded administration of interventions and patient compliance. Yet, into the methodologies of neither Bai et al. (2012) nor Zhu et al. (2023) is mentioned anything regarding: the exact randomization methods adopted; single or double blinding of assessors and/or participants involved; and an appropriate statistical analysis in particular-intention-to-treat methods.

Figure 4. Risk of bias assessments for studies on outcomes of early rehabilitation vs control groups



The high level of heterogeneity found (I2 = 76–78% for motor function and ADLs at 1 month) suggests that differences between studies may have a real impact on the combined results. The dataset was too small for formal subgroup analyses, but possible reasons for the variation include differences in rehabilitation practices by region, participant age and stroke severity, and study quality. Future research with more data could group studies by region, age, or study quality (such as low versus unclear or high risk of bias) to see if certain groups benefit more from early rehabilitation.

A review of risk-of-bias ratings shows that two studies (Liu et al., 2014; Yen et al., 2019) had low risk in most areas. The other two studies (Bai et al., 2012; Zhu et al., 2023) had unclear or high risk because they did not clearly report how they randomized participants, whether they used blinding, or if they included intention-to-treat analysis. This difference in study quality probably added to the variation between results and should be kept in mind when looking at the combined findings.

DISCUSSION

The present meta-analysis offers an overview of the possible effectiveness of early rehabilitation in motor function and ADLs during the acute phase after ICH. Indeed, as immediate rehabilitation was initiated, the better the motor outcome and function independence were observed in the early stages of the recovery process. On the other hand, besides differences in designs and methodologies, the results open other avenues to important questions on the long-term sustainability of benefits.

Recovery of the Motor Function

Early rehabilitation in the meta-analysis resulted in a moderate improvement in motor function represented by an SMD of 0.55, as measured by FMA and FAC, with a 95% CI of 0.09 to 1.00, p value 0.02. The size of this effect suggests that early rehabilitation results in significantly higher motor recovery compared to standard care. As might be expected, exclusion of the study by Bai et al. (2012) resulted in an even stronger effect: SMD = 0.79, 95% CI 0.45, 1.13, $p < 0.00001$, and provided evidence that the quality and rigor of individual studies could be highly influential for the overall findings. Larger effects in the studies by Yen et al. and Zhu et al. support the potential benefit of early intervention, but these findings are importantly tempered by the considerable heterogeneity across studies ($I^2 = 76\%$, p = 0.02).

Such heterogeneity in motor function outcomes may be due to differences in rehabilitation protocols, characteristics of the patients, timing of intervention, and specific motor assessments used.

For instance, the intensity, frequency, and duration of the rehabilitative exercises may result in differences in the outcomes measured. Differences in the populations included in the studies, regarding the severity of ICH, are also a potential source of heterogeneity. Moreover, post-intervention time points of assessment may also contribute to the presence of heterogeneity among these studies, regarding when the post-measurements take place earlier or later than the rest. These features again bring into focus the need for standardized rehabilitation protocols and similar types of study design to provide an appropriate understanding of the influence of early rehabilitation upon motor functions.

When beginning early rehabilitation, patient safety should come first. For people with acute intracerebral hemorrhage (ICH), keeping blood pressure steady can help prevent hematoma expansion. Studies suggest that starting rehab within 24 to 72 hours is safe for patients with mild to moderate ICH if certain conditions are met. These include keeping systolic blood pressure between 140 and 160 mmHg, making sure there is no neurological decline, and confirming that imaging does not show hematoma growth. Blood pressure should be checked regularly during early movement, and activity should stop if systolic blood pressure rises above 180 mmHg, falls below 100 mmHg, or if new neurological symptoms appear. These safety limits are important to remember when considering early rehabilitation.

Activities of Daily Living (ADLs)

An improvement in ADLs, measured by the MBI and FIM-motor, was also observed at 1 month post-initiation of rehabilitation, with an SMD of 0.57 (95% CI 0.10, 1.05, p = 0.02). However, this effect did not continue at 3 months, SMD = 0.17, 95% CI 0.00, 0.35, p = 0.05, perhaps suggesting that the benefits of early rehabilitation may be more immediate and potentially diminish over time. The fact that at 1 month, after the exclusion of the Bai et al. study (2012), the effect size was stronger (SMD = 0.82, 95% CI 0.48, 1.16, $p < 0.00001$), underlines once more the fact that methodological quality influences study outcomes.

The similar findings at 3 months, as evidenced by a low I^2 of 14% (p = 0.31), suggest that in the short-term, this variability reduces further in ADL outcomes; however, this does not equate to functional benefits that are similarly sustained.

This transient nature of improvement in ADLs gives rise to some crucial implications for clinical practice. Although this appears to be an initial boost for functional independence, it lacks sustained effects at 3 months, which may indicate the necessity for ongoing or additional interventions. This finding aligns with other research suggesting that stroke rehabilitation is most effective when it is continuous and adaptive toward the patient's recovery trajectory.

Future trials should address whether the extension of duration or change in intensity of early rehabilitation can maintain the gains in ADLs beyond the early post-stroke period.

It is also important to consider that safe early rehabilitation is dependent on adherence to strict blood pressure monitoring protocols. Mobilization shortly after ICH can lead to transient blood pressure surges; thus rehabilitation teams often employ stepwise activity progression with pre- and post-mobilization BP checks, continuous monitoring during the first mobilization session, and deferral of therapy when hemodynamic instability is present. These physiologic considerations may influence both the feasibility and timing of ADL recovery observed in the included studies.

Methodological Considerations and Quality of Study

The considerable heterogeneity obtained in this meta-analysis, especially in the motor function and ADLs analysis at 1 month, underlines heterogeneity in the design of studies, patient populations, and the intervention protocols themselves. This makes the interpretation of these results more difficult and points out, with growing urgency, the need for more standardized and well-designed studies.

After the assessment of the risk of bias, there was appropriate documentation that studies by Liu et al. (2014) and Yen et al. (2019) presented good methodologies, with sufficient randomization, blinding, and statistical analyses. On the other hand, Bai et al. (2012) and Zhu et al. (2023) lacked the crucial information about the randomization method, blinding, and the intention-to-treat analysis. These methodological deficiencies likely contributed to the heterogeneity observed and may have biased test results in favor of early rehabilitation. High heterogeneity and variable quality of included studies underpin further rigorous research in this area. Future trials should be designed with standard protocols in terms of randomization, blinding, and statistical analysis in order to reduce bias and enhance the reliability of findings. Authors may also consider stratification of patients according to stroke severity, age, and comorbidities to better understand which subgroup of patients would benefit the most with early rehabilitation.

Alignment with Established Clinical Guidelines

The results of this meta-analysis partly match the current AHA/ASA guidelines for spontaneous intracerebral hemorrhage (ICH). These guidelines suggest starting early rehabilitation once patients are medically and neurologically stable. They advise against mobilizing patients in the first 24 hours because of the risk of hemodynamic instability. Instead, mobilization is recommended after 24 to 48 hours, as long as blood pressure is controlled and neurological status is monitored. The studies reviewed here, especially those showing that early rehabilitation within 24 to 72 hours is safe, support these guidelines. The evidence also highlights the importance of careful blood pressure management and monitoring. Using guideline-based criteria in future clinical trials would make results easier to compare and help build stronger evidence about the best time to start rehabilitation.

Clinical Implications and Future Directions

The current findings carry significant clinical practice implications. Although early rehabilitation seems to be associated with short-term gains in both motor function and ADL independence, the maintenance of effects thereafter, specifically for ADL independence is confounded, suggesting the long-term benefits of early intervention alone should be approached with more caution by the clinician. The findings suggest that continuing rehabilitation strategies adapted beyond the immediate post-stroke period would have optimized functional recovery and long-term outcomes.

Future studies should overcome these methodological limitations indicated by this meta-analysis and should evaluate the mechanisms for such great variability in patients' responses to early rehabilitation. Only a clearly focused study regarding the timing, intensity, and duration of the rehabilitative intervention, and characteristics of patients most likely to benefit, will lead to a refinement of clinical guidelines and improved care for patients. There is also a need for further research into the long-term effects of early rehabilitation on the quality of life, cognitive function, and participation in social and community activities.

Using standardized safety criteria, especially for blood pressure limits, hemodynamic stability, and timing of follow-up imaging, is important for making early rehabilitation practices safer and more consistent. Future studies should clearly describe their mobilization safety protocols to help with comparison and support evidence-based clinical practice.

CONCLUSION

This meta-analysis shows that starting rehabilitation within 72 hours after ICH can improve motor recovery and independence in daily activities at one month. However, it is still uncertain whether these benefits last at three months. The evidence points to short-term functional gains, but the long- term effects on daily activities are less clear, partly because the studies included were quite different and varied in quality. Early rehabilitation within 24 to 72 hours seems safe and helpful when patients are medically and hemodynamically stable, so it may be cautiously added to acute ICH care. Using standardized early-mobilization protocols, especially those that include blood pressure monitoring and checks for neurologic stability, along with ongoing rehabilitation after the acute phase, may help improve outcomes. More consistent and well-designed studies are needed to determine the best timing, safety measures, and rehabilitation approaches, and to better understand why patient responses differ across current research.

REFERENCES

1. Asch, C., Luitse, M., Rinkel, G., Tweel, I., Algra, A., & Kilijin, C. (2010, January 5). Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: A systematic review and meta-analysis. PUBMED. https://pubmed.ncbi.nlm.nih.gov/20056489/
2. Bai, Y., Hu, Y., Wu, Y., Zhu, Y., He, Q., Jiang, C., Sun, L., & Fan, W. (2012, July 18). A prospective, randomized, single-blinded trial on the effect of early rehabilitation on daily activities and motor function of patients with hemorrhagic stroke. PUBMED. https://pubmed.ncbi.nlm.nih.gov/22819061/
3. Liu, N., Cadilhac, D., Andrew, N., Zeng, L., Li, Z., & Li, J. (2014, October 21). Randomized Controlled Trial of Early Rehabilitation After Intracerebral Hemorrhage Stroke: Difference in Outcomes Within 6 Months of Stroke. Ahajournals.org. https://www.ahajournals.org/doi/10.1161/strokeaha.114.005661
4. Yen, H. C., Jeng, J. S., & Chen, W. S. (2019, December 20). Early Mobilization of Mild-Moderate Intracerebral Hemorrhage Patients in a Stroke Center: A Randomized Controlled Trial. Pubmed. https://pubmed.ncbi.nlm.nih.gov/31858865/

5. Zhu, F., Fan, S., & Liu, G. (2023, December 5). Effect of early rehabilitation training on motor function and neural function of patients with brainstem hemorrhage after body-oriented individualized surgery. Yiigle. https://rs.yiigle.com/cmaid/1481521
6. Hemphill, J. C., III, Greenberg, S., & Anderson, C. (2015, May 28). Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Ahajournals. https://www.ahajournals.org/doi/10.1161/str.0000000000000069
7. Yen, H. C., Jeng, J. S., Cheng, C. H., Pan, G. S., & Chen, W. S. (2015, May 28). Effects of early mobilization on short-term blood pressure variability in acute intracerebral hemorrhage patients: A protocol for randomized controlled non-inferiority trial. Pubmed. https://pubmed.ncbi.nlm.nih.gov/34032760/
8. Marek, K., Zielinska-Nowak, E., Redlicka, J., Starosta, M., & Miller, E. (2024, June 27). Intracranial Hemorrhage-Is Very Early Rehabilitation Safe? A Narrative Review. Pubmed. https://pubmed.ncbi.nlm.nih.gov/38999342/
9. Liu, L., Lu, Y., Bi, Q., Fu, W., Zhou, X., & Wang, J. (2021, August 28). Effects of Different Intervention Time Points of Early Rehabilitation on Patients with Acute Ischemic Stroke: A Single-Center, Randomized Control Study. Pubmed. https://pubmed.ncbi.nlm.nih.gov/34493977/
10. Liu, Y., Yin, J.-H., Lee, J.-T., Peng, G.-S., & Yang, F.-C. (2022, January 18). Early rehabilitation after acute stroke:the golden recovery period. Acta neurologica Taiwanica. https://pubmed.ncbi.nlm.nih.gov/34918304/
11. Langhorne, P., Wu, O., Rodgers, H., Ashburn, A., & Bernhardt, J. (2017). A very early rehabilitation trial after stroke (avert): A Phase III, Multicentre, randomised controlled trial. Health Technology Assessment, 21(54), 1–120. https://doi.org/10.3310/hta21540
12. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.
13. McGrath S., Zhao X., Steele R., Thombs B.D., Benedetti A., and the DEPRESsion Screening Data (DEPRESSD) Collaboration. (2020). Estimating the sample mean and standard deviation from commonly reported quantiles in meta-analysis. Statistical Methods in Medical Research, 29(9), 2520–2537. https://doi.org/10.1177/0962280219889080