Effects of Early Mobilization after Acute Stroke: A Meta-Analysis of Randomized Control Trials

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Background: Early mobilization is inconsistently associated with the recovery of stroke. We aim to examine the effect of early mobilization on patients with acute stroke. *Methods:* PubMed, EMBASE, and the Cochrane library were searched up to April 2017. Randomized controlled trials that reported risk estimates or mean with standard deviation were included. Primary outcomes were defined as modified Rankin scale score 0-2 and mortality, and secondary outcomes were Barthel Index, length of stay, and incidence of complications. Summary relative risk, standardized mean difference (SMD), and weighted mean difference (WMD) were calculated as needed. Sensitivity analyses were also conducted to test stability of results. *Results:* Six studies (8 publications) were included to analyze the effects of early mobilization after stroke. No differences between groups were observed for modified Rankin scale 0-2 (relative risk [RR]: .80; 95% confidence interval [CI]: .58-1.02; $I^2 = 45\%$) and the risk of death (RR: 1.21, 95% CI: .76-1.65; $I^2 = 0\%$). Compared with conventional practice, early mobilization was superior in Barthel Index (SMD: .66; 95% CI: .00-1.31; $I^2 = 85.9\%$), and shorter hospital stay for stroke patients (WMD: −1.97; 95% CI: −2.63 to −1.32; $I^2 = 15.3\%$). We found no significant difference between groups on the incidence of complications. *Conclusions:* Current evidence revealed that no statistical significant difference between early mobilization and non-early mobilization was observed on modified Rankin scale score 0-2 and mortality. Interestingly, early mobilization is associated with an increased Barthel Index and shorter hospital stay for patients. Further research is necessary to verify the effect of early mobilization on patients with acute stroke.
Key Words: Early mobilization—stroke—modified Rankin scale—mortality—self-care ability—rehabilitation—Barthel Index.

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Introduction

Stroke is one of the most important causes of death and long-term disability around the world, and developing countries show heavier burden of stroke than developed countries.[1,2] Given the burden of stroke, nearly 800,800 individuals were affected by stroke annually and many survivors suffer constant difficulty with daily tasks.[3] Immediate admission, tissue plasminogen activator. and early mobilization (EM) have been proposed, which were beneficial for prognosis of patients with stroke.[4] EM has attracted much attention recently in the clinical research field,[5,6] which is a procedure to accelerate the ability of patients to walk or move, which is characterized by a shorter period of hospitalization or recumbency than normally practiced, such as early sitting out of bed, transfer, standing, and walking.[7-16]

Some studies showed a positive effect of EM,[14,15,17] whereas others revealed inconsistent and controversial findings.[7,8] A 2008 phase II clinical trial conducted by Bernhardt et al[17] revealed that EM within 24 hours appeared to be safe and feasible for stroke patients and improved their independence in activities of daily living. Meanwhile, an individual patient data meta-analysis made a comparable conclusion by precise data source.[18] Unexpectedly, an international randomized controlled trial (RCT) involving more than 2000 stroke patients[7] found that EM within 24 hours reduced the odds of a favorable outcome defined as modified Rankin scale (mRS) score 0-2, which might change clinical decision. EM has both potential harm and potential benefits on recovery process post stroke, such as potential aggravation of neurologic deficits[19,20] and preventing immobility-related complications,[21] arising confusion on the topic for patients with acute stroke. Some researchers found that it is not adequate to confirm that EM is beneficial to the recovery of patients with stroke,[22,23] and the evidences need to be further explored.

For these reasons we conducted a systematic review to study this controversial topic and explore the effect of EM post stroke and its impact on prognosis of patients with stroke.

Methods

Search Strategy

The present study was conducted according to the Preferred Reporting Items for Systemic Reviews and Meta-Analyses statement.[24] We conducted a comprehensive electronic search to obtain relevant RCTs published from 1970 to April 2017 on PubMed, EMBASE, and the Cochrane Library. Supplement Table S1 in the online-only data showed the search strategy in detail. Both free text and explored Medical Subject Headings terms were used as follows: "stroke," "cerebrovascular accident," "early mobilization," "early rehabilitation," "early ambulation," "modified Rankin scale," "mortality," "Barthel Index," "functional independence measure," "length of stay," and "outcome assessment." We do not attempt to get unpublished papers, and we manually checked the reference lists from included studies and relevant reviews to identify additional citations.

Study Selection

Trails were included if they met the following characteristics: (1) population—patients with acute ischemia or hemorrhagic stroke; (2) intervention—EM within 24 hours post stroke (consensus definition of start time for EM was inadequate, therefore we definite it as 24 hours.); (3) control—non-EM protocols (e.g., delayed mobilization, usual care); (4) outcomes—mRS score 0-2 and mortality were considered as primary outcomes for this meta-analysis, secondary outcomes included Barthel Index (BI), length of stay (LOS), and incidence of complications; and (5) study design—RCT. Study screening was conducted by a 2-stage method. First, titles and abstracts were scrutinized to exclude ineligible studies. Second, investigators read the full texts for including eligible studies. Any disagreements on study screening were resolved by discussions.

Data Extraction and Quality Assessment

In the present study, data extraction was performed by investigators (L.Z.Y. and W.K.) as follows: first author, publication year, study location, participant's mean age, sample size, stroke type, intervention protocol, control protocol, the first out-of-bed activities time, outcomes, mean and standard deviation for continuous variable, and risk estimate with corresponding 95% confidence interval (CI) for binary variable. Median with range was extracted when initial study did not report mean and standard deviation.

We appraised quality of each research by the "risk of bias" tool, which was recommended by the Cochrane Handbook,[25] and quality scores were assigned for (1) random sequence, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other bias.

The quality of evidence for each outcome was graded according to GRADE guideline.[26] We assessed downgrading factors including risk of bias, inconsistency of results, indirectness of evidence, imprecision, as well as publication bias, and upgrading factors comprising large magnitude of effect, plausible confounding factors would change the effect, and dose-response gradient, respectively. According to evaluation, quality of evidence was judged as "very low," "low," "moderate," or "high."