

Original Article

Head positioning in suspected patients with acute stroke from prehospital to emergency department settings: a systematic review and meta-analysis

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Aim: This study aimed to clarify whether the lying-flat position from prehospital to emergency department settings more effectively improves neurological outcomes of patients suspected with acute stroke over the sitting-up position.

Methods: We searched PubMed, the Cochrane Central Register of Controlled Trials, and Igaku Chuo Zasshi for published randomized controlled trials until September 2019. The study population included patients suspected with acute stroke from prehospital to emergency department settings. We compared outcomes between the lying-flat position and sitting-up position groups. The critical outcome was the modified Rankin Scale score at 90 days, and important composite outcomes were 90-day mortality, pneumonia recurrence, and recurrent ischemic stroke. The certainty of evidence of the outcome level was compared using the Grading of Recommendations Assessment, Development, and Evaluation approach.

Results: In total, 881 studies were identified from the databases, and two randomized controlled trials were included in the analysis. The pooled risk ratio of 90-day modified Rankin Scale score was not statistically significant (risk ratio 0.86; 95% confidence interval [CI] 0.56–1.32) between the lying-flat position and sitting-up position groups. When comparing the 90-day mortality, pneumonia occurrence, and recurrent ischemic stroke, no significant differences were observed between the two groups. Risk ratio was 1.00 (95% CI 0.87–1.14), 0.90 (95% CI 0.74–1.11), and 0.81 (95% CI 0.14–4.64) for 90-day mortality, pneumonia occurrence, and recurrent ischemic stroke, respectively.

Conclusion: This study suggests that the lying-flat position is not more effective than the sitting-up position in terms of 90-day modified Rankin Scale score in patients suspected with acute stroke.

Key words: Head position, ischemic stroke, pneumonia, stroke

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INTRODUCTION

OWING TO THE aging society, by the year 2050, the number of stroke events will expand 2.25 times compared with that in 2010 worldwide.¹ Apparently, appropriate management not only in the acute phase of hospitalization but also in prehospital settings is required to improve the neurological outcomes of stroke patients. With regard to the head positioning of stroke patients, although the lying-flat

position increases cerebral blood flow,² a potential risk of aspiration pneumonia exists.³

The American Heart Association (AHA)/American Stroke Association (ASA) recently published the guideline and provided the recommendation that the benefit of flat-head positioning early after hospitalization for stroke remains uncertain in patients with acute ischemic stroke.⁴ However, systematic reviews and meta-analyses have not been performed in the recommendation,⁴ and whether the lying-flat position more effectively improves neurological outcomes than the sitting-up position in patients suspected with acute stroke from prehospital to emergency department (ED) settings remains unknown.

Therefore, this study aimed to clarify whether the lying-flat position from prehospital to ED settings improves the neurological outcomes of patients suspected with acute stroke compared with the sitting-up position by conducting a systematic review and meta-analysis.

METHODS

THIS SYSTEMATIC REVIEW and meta-analysis protocol has been registered in PROSPERO, an International Prospective Register of Systematic Reviews of the National Institute for Health Research and Center for Reviews and Dissemination (CRD) at the University of York (<http://www.crd.york.ac.uk/PROSPERO/>; registration no. CRD42020149351).

The systematic review and meta-analysis were reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)^{5,6} and do not require ethical approval.

Search strategies

Databases such as MEDLINE (via PubMed), the Cochrane Central Register of Controlled Trials, and Iqaku Chuo Zasshi were searched to retrieve relevant articles for the literature review. We searched for full-text randomized controlled trials (RCTs) published until September 2019. We used a combination of key terms and established a full search strategy (Table S1).

Study selection and inclusion criteria

The study population of interest was patients suspected with acute stroke from prehospital to ED settings. We did not restrict our analysis by country and included all severities and types of stroke. Conference abstracts and animal studies were excluded, and we only included studies that were written in English or Japanese.

The interventions of interest are the lying-flat and sitting-up positions. For the lying-flat position, patients were positioned at 0° and then maintained in this position for the next 24 h, whereas for the sitting-up position, the head of the patient was elevated to at least 30°. We compared the outcomes between the lying-flat and sitting-up position groups. The critical outcome in the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was the modified Rankin Scale (mRS) score at 90 days,⁷ whereas the important composite outcomes in the GRADE system were 90-day mortality, pneumonia occurrence, and recurrent ischemic stroke.

Risk of bias assessment

To assess the quality of the included studies, the Cochrane and GRADE system risk of bias tool were adopted.⁸ Each study was assessed for (i) random sequence generation (selection bias), (ii) allocation concealment (selection bias), (iii) blinding of participants and personnel (performance bias), (iv) blinding of related outcome assessment (detection bias), (v) incomplete outcome data (attrition bias), (vi) selective reporting (reporting bias), and (vii) others. Studies were categorized as having a low, unclear, or high risk of bias in each domain. The risk of bias for each element was considered “high” when bias was present and likely to affect outcomes and considered “low” when bias was absent or present but unlikely to affect outcomes.⁹

Two independent reviewers (TO and DS) chosen by the authors performed the risk of bias assessment. Disagreements were resolved via discussions.

Data extraction and management

The following data were extracted: author(s), title, journal name, year of publication, website (URL), and abstract. After removing duplicates, two independent reviewers (TO and DS) screened the abstracts and titles of the studies and subsequently reviewed the full-text articles. Disagreements were reconsidered and discussed until a consensus was reached. The full text of the articles included in the final selection was independently reviewed by another two reviewers (TO and DS). Disagreements were solved by a third reviewer (TH). The flow diagram of our study, adapted from the PRISMA statement, is shown in Figure 1.

Rating the certainty of evidence using the GRADE approach

We used the GRADE tool to rate the quality of evidence on the effect of the lying-flat and sitting-up position groups on

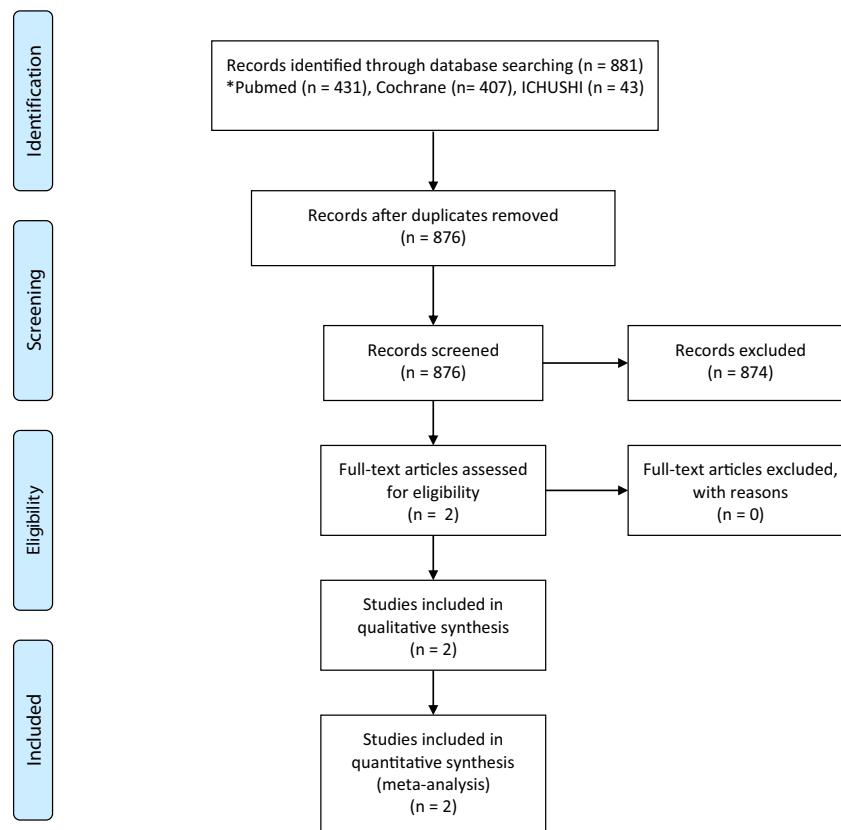


Fig. 1. Flow chart of the study selection process.

important outcomes in patients suspected with acute stroke.^{10–13} The certainty of evidence was assessed for each outcome and categorized as high, moderate, low, or very low using the GRADEpro Guideline Development Tool.

Statistical analysis

We performed a meta-analysis because one or more data were available according to the “Cochrane Handbook for Systematic Reviews of Interventions” and PRISMA guidelines. Results were summarized using a random effects model to facilitate pooling of treatment effect estimates. Risk ratios (RRs) and 95% confidence intervals (CIs) were used for dichotomous outcomes.

Heterogeneity between trials for each outcome was evaluated using the I^2 statistics to quantify inconsistency.¹⁴ Heterogeneity was considered being significant if the reason for heterogeneity could not be explained as well as if I^2 was 50% or more.

Regarding the assessment of reporting bias, a funnel plot was performed to investigate the potential for publication

bias. Estimates were pooled using a random effects model. A meta-analysis was performed based on all published data and data made available to us.⁹

All analyses were performed using the Review Manager software (RevMan 5.3, Copenhagen, Denmark: The Nordic Cochrane Centre, the Cochrane Collaboration 2014).

RESULTS

Literature search

WE IDENTIFIED 881 studies from the electronic databases. Five duplicates and 876 studies were excluded because their design was not fitted. Finally, two studies were retained for review of the full-length reports; these two studies^{15,16} were included in the final analysis (Fig. 1).

Study characteristics

The two RCTs^{15,16} included 11,187 patients: 5,338 were assigned to the lying-flat position group and 5,849 to the

Table 1. Baseline characteristics of eligible studies

No.	Author (year) ^{Reference}	Number of included patients	Setting	Type of stroke	NIHSS (median)		Degree		Time to onset of intervention (median, h)	
					Lying flat	Sitting up	Lying flat	Sitting up	Lying flat	Sitting up
1	Olavarria <i>et al.</i> (2018) ¹⁵	94	Within 12 h of symptom onset	Acute ischemic stroke	6	7	0°	Head up to 30° or more	5.5	5.0
2	Anderson <i>et al.</i> (2017) ¹⁶	11,093	Emergency department Inpatient service	TIA Acute ischemic stroke Primary intracranial hemorrhage Stroke mimic	4	4	Lie fully supine	At least 30°	14	14

NIHSS, National Institutes of Health Stroke Scale; TIA, Transient ischemic attack.

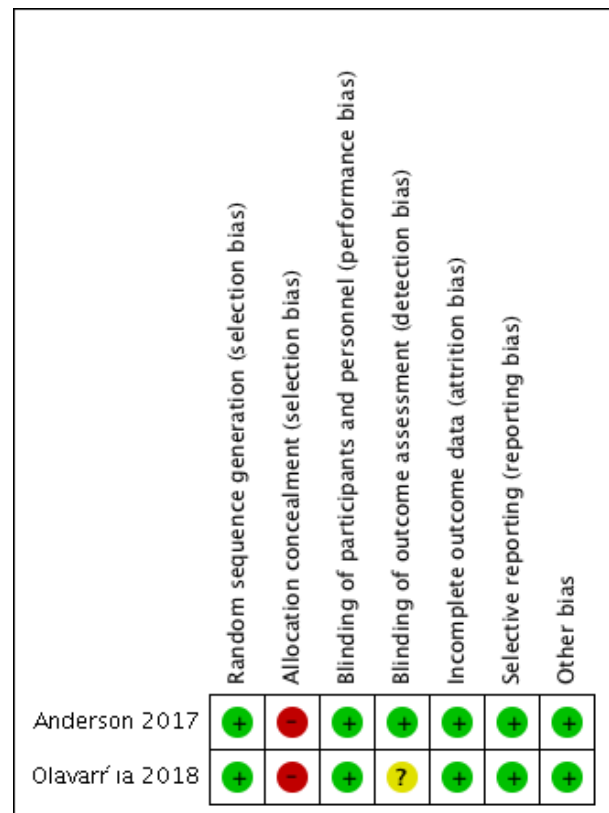
sitting-up position group. Individual characteristics of the trials included in this meta-analysis are detailed in Table 1. The risk of bias was evaluated in each study and is shown in the risk of bias summary in Figure 2.

Outcomes

A total of 9,832 patients (two studies) reported mRS score at 90 days as a critical outcome and were divided into 4,719 for the lying-flat position and 5,113 for the sitting-up position groups (Fig. 3A). Among them, 1,826 patients developed mRS score of 3–6 in the lying-flat position and 2,027 patients developed mRS score of 3–6 in the sitting-up position group. However, the pooled RR of mRS score at 90 days was not statistically significant (RR 0.86; 95% CI 0.56–1.32; Fig. 3A). When comparing the 90-day mortality, pneumonia occurrence, and recurrent ischemic stroke, no significant differences were observed between the lying-flat position and sitting-up position groups. The pooled RR was 1.00 (95% CI 0.87–1.14), 0.90 (95% CI 0.74–1.11), and 0.81 (95% CI 0.14–4.64) for 90-day mortality (Fig. 3B), pneumonia occurrence (Fig. 3C), and recurrent ischemic stroke (Fig. 3D), respectively.

Heterogeneity

Although no statistically significant heterogeneity in mRS score at 90 days was observed between the lying-flat

**Fig. 2.** Risk of bias summary of the included studies.

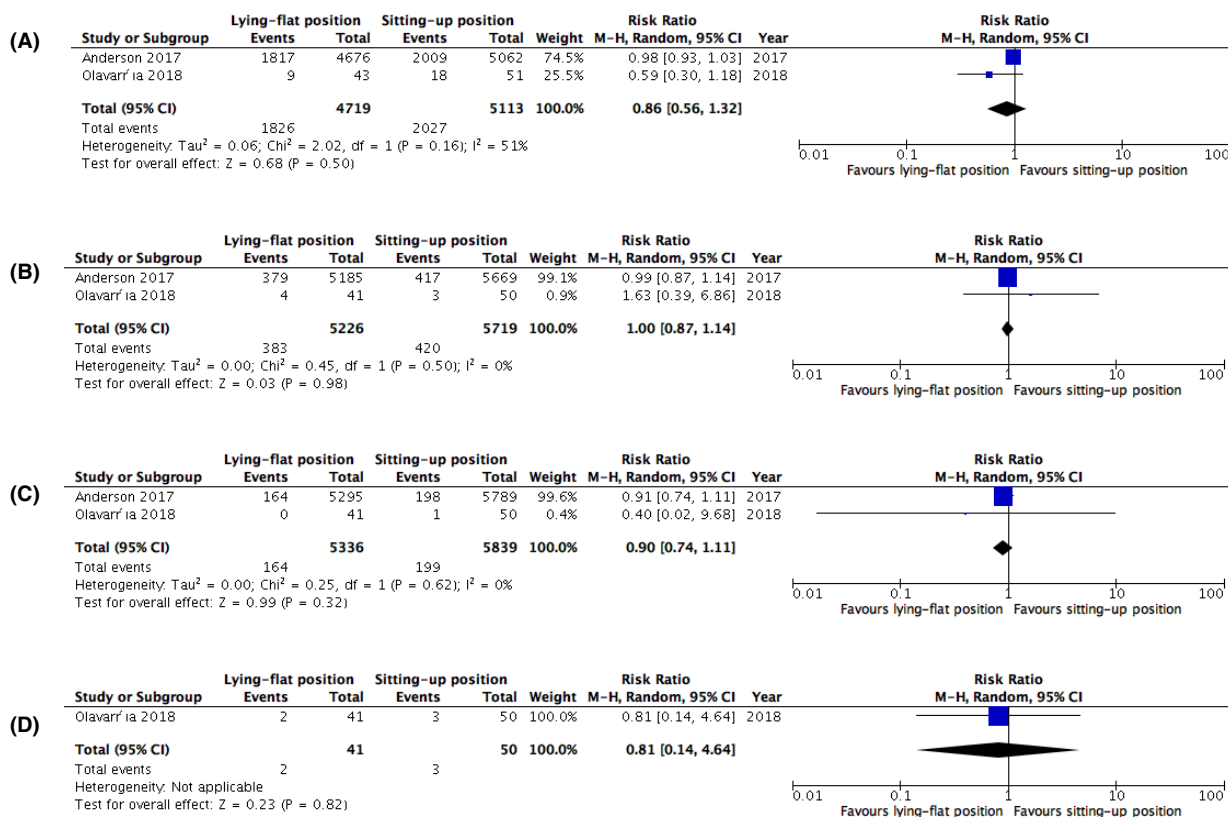


Fig. 3. Forest plot of the comparison. A, Lying-flat position versus sitting-up position for modified Rankin Scale score at 90 days. B, Lying-flat position versus sitting-up position for mortality at 90 days. C, Lying-flat position versus sitting-up position for pneumonia occurrence. D, Lying-flat position versus sitting-up position for recurrent stroke infarction. CI, confidence interval; M-H, Mantel-Haenszel method.

position and sitting-up position groups, inconsistency was judged to be serious due to I^2 being 50% or more ($I^2 = 51%$; $\chi^2_1 = 2.02$; $P = 0.16$). In addition, no statistically significant heterogeneity in 90-day mortality and pneumonia occurrence was observed between the lying-flat position and sitting-up position groups ($I^2 = 0%$; $\chi^2_1 = 0.45$; $P = 0.50$, $I^2 = 0%$; $\chi^2_1 = 0.25$; $P = 0.62$, respectively).

Publication biases and certainty of evidence

We tested for the presence of publication biases as the primary outcome. A visual inspection of the funnel plots suggested no existence of publication biases on mRS score at 90 days (Fig. S1).

The certainty of evidence was rated as low due to serious inconsistency and imprecision for the effect of the lying-flat position on mRS score at 90 days compared with the sitting-up position. The certainty grade in 90-day hospital mortality was rated as high. The certainty of evidence was rated as moderate for the effect of the lying-flat position on

pneumonia occurrence compared with the sitting-up position because imprecision was judged to be serious. The certainty of evidence was rated as moderate due to the judgment of serious imprecisions for the effect of the lying-flat position on recurrent ischemic stroke compared with the sitting-up position (Table 2).

DISCUSSION

IN THIS SYSTEMATIC review, the available evidence comparing the sitting-up position group with the lying-flat position group was summarized, showing no significant improvements on mRS scores at 90 days, mortality at 90 days, pneumonia occurrence, and recurrent ischemic stroke in patients suspected with acute stroke.

Our results are consistent with AHA/ASA's recommended published guidelines targeting in-hospital patients with acute ischemic stroke.⁴ However, acute ischemic stroke cannot be reliably determined in prehospital settings given the currently available routine diagnostic tools.¹⁷ All

Table 2. Summary of findings

Certainty assessment		No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
			Lying-flat position	Sitting-up position	Relative (95% CI)	Absolute (95% CI)	
mRS at 90 days							
2	Randomized trials	Not serious	Serious [†]	Not serious	Serious [‡]	None	
			1,826/4,719 (38.7%)	2,027/5,113 (39.6%)	RR 0.86 (0.56 to 1.32)	56 fewer per 1,000 (from 174 fewer to 127 more)	⊕⊕○○ LOW Critical
Mortality at 90 days							
2	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	
			383/5,226 (7.3%)	420/5,719 (7.3%)	RR 1.00 (0.87 to 1.14)	0 fewer per 1,000 (from 10 fewer to 10 more)	⊕⊕⊕⊕ HIGH Critical
Pneumonia							
2	Randomized trials	Not serious	Not serious	Not serious	Serious [‡]	None	
			164/5,336 (3.1%)	199/5,839 (3.4%)	RR 0.90 (0.74 to 1.11)	3 fewer per 1,000 (from 9 fewer to 4 more)	⊕⊕⊕○ MODERATE Critical
Recurrent ischemic stroke							
1	Randomized trials	Not serious	Not serious	Not serious	Serious [‡]	None	
			2/41 (4.9%)	3/50 (6.0%)	RR 0.81 (0.14 to 4.64)	11 fewer per 1,000 (from 52 fewer to 218 more)	⊕⊕⊕○ MODERATE Critical

CI, confidence interval; mRS, modified Rankin Scale; RR, risk ratio.

[†] $I^2 = 51\%$.[‡]Insufficient sample size.

subtypes of stroke were included in our eligible studies and were not limited to ischemic stroke (depends on the final diagnosis, which is very critical).

Our findings showed that the lying-flat position did not have advantages over the sitting-up position. One of the possible reasons is that one of the two studies weighted at least 75% in each outcome, including patients with minor strokes (median National Institutes of Health Stroke Scale score of 4 in both groups) who might have been less likely to benefit from increased perfusion (i.e., lying-flat position) compared with patients with more severe strokes.¹⁶ Moreover, the median time from stroke onset to intervention was relatively late (median, 14 h in both groups) in this study, making the lying-flat position less beneficial.¹⁶

The effects of the lying-flat position have not been clearly elucidated, indicating the need for larger and more randomized trials. Another randomized trial investigating the effect of head down procedures at -20° in the supine position for acute ischemic stroke patients is currently ongoing in China (NCT03744533). The primary outcome for the study is mRS score of 0–2 at 90 days. The result of this study may indicate the benefit of more aggressive head positioning in patients with acute ischemic stroke. Considering the clinical implementation under the current limited clinical evidence, both positions (lying-flat and sitting-up positions) are acceptable in the clinical practice of prehospital settings. That is, it is inappropriate to recommend only one position (lying-flat or sitting-up position) in all situations. The lying-flat position can be chosen based on the pathophysiology of acute stroke; however, the sitting-up position might be considered in limited situations such as in patients strongly suspected with the Cushing phenomenon or severe aspiration pneumonia.

Limitations

This study has several limitations. First, the meta-analysis was based on data from only two RCTs, which are insufficient to obtain more robust conclusions. This indicates the need for larger and more randomized trials. Another randomized trial investigating the effect of head down procedures at -20° in the supine position for acute ischemic stroke patients is currently ongoing. We hope that researchers are aware of the problem throughout this study, and that this study will lead to further RCTs. Second, studies in prehospital settings were not identified through current search strategies. Third, we could not perform subgroup analysis that divides included patients into types of stroke because of insufficient data in the included studies. Fourth, in the current meta-

analysis, the sitting-up position was defined as the elevation of the head of the patient to at least 30° in our eligible studies,^{15,16} and milder sitting-up positions, such as at 15° and 20° , were not evaluated. Fifth, although cluster-randomized, crossover trials were conducted to exclude potential bias, variability of treatment between centers might have contributed to the outcome. Participating institutions followed standards of care recommendation in their own national guidelines; however, details of guidelines may be different.

CONCLUSION

THIS STUDY SHOWS that the lying-flat position does not have any advantages on mRS scores at 90 days, 90-day mortality, pneumonia occurrence, and recurrent ischemic stroke in patients suspected with acute stroke. Further studies are needed to validate our results due to lack of adequate evidence.

DISCLOSURE

Approval of the research protocol: N/A.

Informed Consent: N/A.

Registry and the Registration No. of the study/Trial: CRD42020149351.

Animal Studies: N/A.

Conflict of Interest: None.

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AUTHOR CONTRIBUTIONS

TH CONCEIVED THE idea for this systematic review. TH, KY, DS, and TO developed the methodology. TH drafted the manuscript. KY, DS, TO, HK, JG, KU, YK, and SY revised the manuscript. SY and YK performed critical revision of the manuscript. All authors critically reviewed and approved the final manuscript.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Search strategies on MEDLINE (via PubMed), the Cochrane Central Register of Controlled Trials, and Igaku Chuo Zasshi.

Figure S1. The funnel plots on mRS at 90 days.