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Original Article

The Impact of the Total Amount of Exercise Therapy on Post-Stroke Activities of Daily Living and Motor Function: A Meta-Analysis

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HIGHLIGHTS

- More exercise time improves daily living activities compared to less time spent.
- Higher intensity exercise enhances lower limb function more than lower intensity.
- Increasing exercise is recommended, tailored to individual conditions post-stroke.

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The authors have no potential conflicts of interest to disclose.

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ABSTRACT

Although the benefits of exercise therapy in stroke rehabilitation are well-documented, the optimal amount remains a matter of debate. This study investigated the impact of the total amount of exercise therapy on clinical outcomes in adult patients with stroke. We conducted a comprehensive search of three major international databases (Medline, Embase, and the Cochrane Library) and included 18 randomized controlled trials that compared the effects of different amounts of exercise therapy on activities of daily living, upper limb function, lower limb function, and adverse events in stroke patients. We performed a risk of bias assessment, conducted a meta-analysis using a random-effects model, and evaluated the certainty of the evidence. The results indicated that more time spent in exercise therapy significantly improved activities of daily living compared to less time (standardized mean difference [SMD], 0.18; 95% confidence interval [CI], 0.06, 0.30; $p = 0.002$), with moderate evidence. Additionally, higher intensity of exercise therapy enhanced lower limb function compared to lower intensity (SMD, 0.66; 95% CI, 0.18, 1.13; $p = 0.007$), with a low level of evidence. No significant differences were found in the incidence of adverse events. Based on these findings, physicians may consider increasing the total amount of exercise therapy for stroke patients in order to improve their activities of daily living and motor function, while carefully considering each patient's neurological and medical condition.

Keywords: Activities of Daily Living; Exercise Therapy; Recovery of Function; Stroke Rehabilitation; Time

INTRODUCTION

The total amount (dosage) of exercise therapy prescribed in rehabilitation medicine is determined by the frequency, duration, and intensity of the exercise [1,2]. Although the benefits of exercise therapy for stroke patients are well recognized, debate continues regarding the optimal total amount of exercise therapy. Many experts now believe that, barring any contraindications, increasing the total amount of exercise therapy for stroke patients could lead to improved outcomes [2,3]. However, a 2021 Cochrane review indicated that increasing the duration of the same type of therapy during post-stroke rehabilitation has little to no effect on activities of daily living or on the function of the upper and lower limbs [4].

S, Kim YH; Project administration: Im S, Kim YH; Resources: Im S, Kim YH; Software: Im S, Kim YH; Supervision: Im S, Kim YH; Validation: Im S, Kim YH; Visualization: Im S, Kim YH; Writing - original draft: Im S, Kim YH; Writing - review & editing: Kim YH.

Clinical guidelines from Australia (2017) and Canada (2019) do not include recommendations regarding the total amount of exercise therapy [5,6]. The Clinical Practice Guideline for Stroke Rehabilitation in Korea 2016 strongly recommends increasing the intensity (or amount) of therapy to enhance treatment effects in stroke patients (recommendation level A, evidence level 1+) [7]. However, this earlier guideline conflates terms related to the intensity, frequency, and duration of exercise therapy. Additionally, since the evidence was derived from studies on various types of rehabilitation therapies—including speech therapy, swallowing therapy, and electrotherapy, as well as exercise therapy—the recommendation for the intensity of exercise therapy lacks sufficient support. Therefore, a revision of the recommendation has been deemed necessary to clearly define the amount of exercise therapy.

Disagreements surrounding the optimal amount of exercise therapy arise from challenges in determining the appropriate total amount for stroke patients. The variability in neurological status among stroke patients, influenced by the time elapsed since the stroke, and the high prevalence of comorbid conditions in older patients further complicate efforts to increase the total amount of exercise therapy indefinitely. Additionally, existing studies on this subject often lack clear and consistent definitions regarding the total amount, frequency, intensity, and duration of exercise therapy, which makes it difficult to draw definitive and comprehensive conclusions [4].

To date, it remains unclear whether a higher total amount of exercise therapy offers clinical benefits compared to a lower amount in stroke patients. Therefore, this meta-analysis aims to combine evidence from existing randomized controlled trials (RCTs) to elucidate the impact of the total amount of exercise therapy on clinical outcomes in adult stroke patients aged 18 years and older. Clinical outcomes included activities of daily living, upper limb function, lower limb function, and adverse events.

MATERIALS AND METHODS

Study protocol and review criteria

This meta-analysis was conducted as part of the development of the Clinical Practice Guideline for Stroke Rehabilitation in Korea—Part 1: Rehabilitation for Motor Function (2022) [8]. Although the protocol for this study was not registered on a formal registration website, it was established prior to the meta-analyses during steering meetings for guideline development.

The key question of the present study was articulated as follows: "Does a higher total amount of exercise therapy (Intervention, I) improve activities of daily living, upper limb function, lower limb function, and adverse events (Outcomes, O) in stroke patients aged 18 years and older (Patient, P), compared to a lower total amount of the same exercise therapy (Comparison, C)?" We included RCTs that compared the effects of different total amounts of the same exercise therapy across groups. RCTs that compared different types of exercise or included a control group that did not perform exercise therapy were excluded.

Literature selection and risk of bias assessments

Based on previous studies and clinical practice guidelines [4-10], we identified appropriate search terms. Six literature search specialists conducted the search, which included publications up to February 28, 2022, across three databases: Medline, Embase, and the Cochrane Library. Detailed search terms and strategies are outlined in **Supplementary Table 1**.

The studies included in this analysis were carefully selected according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (**Fig. 1**). Two authors, SI and YHK, independently assessed and chose the relevant studies. Following the final selection of included RCTs, these same authors independently evaluated the RCTs using the Cochrane Risk of Bias 1.0 tool. In cases of disagreement, the authors resolved issues through detailed discussions.

Meta-analysis

A meta-analysis was conducted using Review Manager 5.4 (RevMan, Cochrane Collaboration, Oxford, UK). To estimate heterogeneity across studies, the I^2 statistic was employed, which evaluates the percentage of total variation. Substantial heterogeneity was defined as an I^2 value greater than 50.0%. For the meta-analysis, the finally included RCTs were categorized

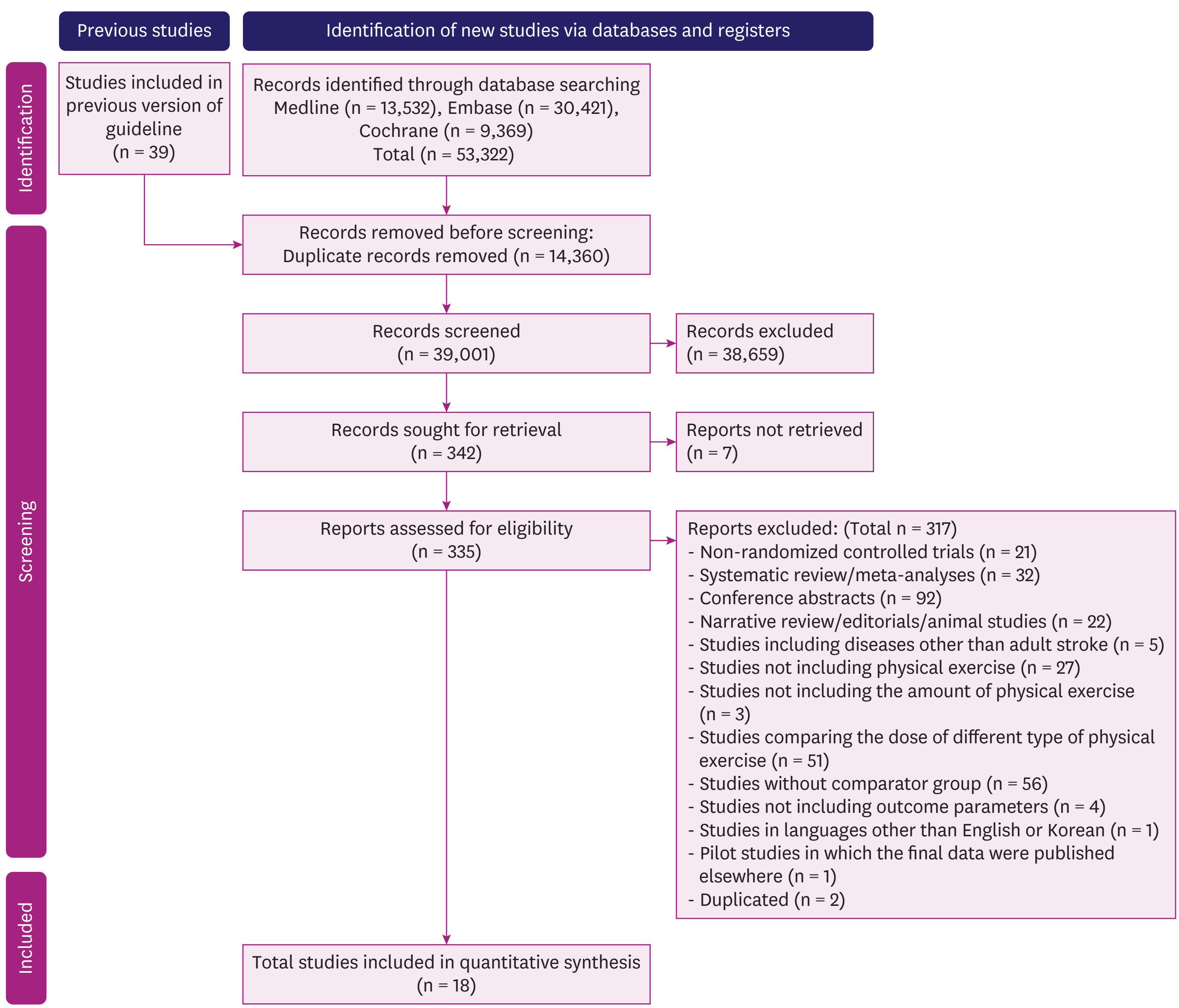

Fig. 1. PRISMA flowchart.
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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into groups according to whether they had a higher or lower total amount (time, intensity) of exercise therapy. The outcome variables of the current study included both continuous (activities of daily living, upper limb function, and lower limb function) and dichotomous (adverse events) variables. During the analyses, continuous outcome variables were analyzed using random effects models with the inverse variance estimation method, and the results were presented as the standard mean difference with 95% confidence intervals (CIs). The dichotomous outcome variable was analyzed using a random effects model with the Mantel-Haenszel estimation method, and the results were presented as risk ratios (RRs) with 95% CIs.

Certainty of evidence evaluation

The certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) method, which categorizes evidence into high, moderate, low, or very low levels [11]. Given that this study exclusively involved RCTs, the initial certainty of evidence was considered high. Subsequently, the level of evidence was adjusted according to the guidelines, either being maintained or downgraded. Factors such as risk of bias, inconsistency, indirectness, imprecision, and publication bias were taken into account during this evaluation. Two authors, SI and YHK, independently assessed the certainty of evidence, and any disagreements were resolved through discussion.

RESULTS

Study characteristics

Following a comprehensive screening of studies using the PRISMA method, we included a total of 18 RCTs in our meta-analyses. Of these, 16 RCTs compared groups that varied in the total amount of exercise therapy, which was determined by modifying the frequency and duration of identical exercises [12-27]. In our analysis, we defined the subgroup that engaged in a higher total amount of exercise therapy as the "more time" subgroup, and the one with a lower total amount as the "less time" subgroup. Two additional studies differentiated subgroups by varying the intensity of the exercises [28,29]. In these cases, the subgroup engaging in a higher total amount of exercise was labeled as the "higher intensity" subgroup, and the one with a lower total amount as the "lower intensity" subgroup. For studies that divided the total amount of exercise into more than two subgroups, we compared the subgroups with the highest and second-highest amounts, based on expert opinion and consensus.

Among the included studies, some reported that increased time spent in exercise therapy led to significant improvements in activities of daily living, upper limb function, and lower limb function compared to those who spent less time in exercise therapy [13-15,18,19,21,25-27]. However, other studies found no significant differences in activities of daily living, upper limb function, and lower limb function between groups that spent more time and those that spent less time in exercise therapy [12,16,17,20,22,23]. The tools used to assess activities of daily living outcome included the Motor Activity Log, Functional Independence Measure, Barthel Index, and Modified Rankin Scale. For upper limb function outcome tool, the Wolf Motor Function Test, Action Research Arm Test, upper extremity items from the Fugl-Meyer Assessment, and the arm section of the Motricity Index were used. Lower limb function outcomes were walking speed, the 6-minute walk test, the Rivermead Mobility Index, and the 5-meter timed walk. The detailed characteristics, including the total amount of exercise therapy and outcome measures for the 18 included studies, are presented in **Supplementary Table 2**. The results of the risk of bias assessment for all included studies are summarized in

Fig. 2. The forest plots of the meta-analyses and the results of the risk of bias assessment for the included studies are shown in **Figs. 3-7**.

Activities of daily living

To evaluate the impact of the amount of exercise therapy on activities of daily living, we analyzed 10 RCTs [12-14,17-19,22,25-27]. As shown in **Fig. 3**, the meta-analysis revealed that more time spent in exercise therapy significantly improved activities of daily living performance compared to the less time group (standardized mean difference [SMD], 0.18; 95% CI, 0.06, 0.30; p = 0.002).

Upper limb function

We analyzed eight RCTs to evaluate upper limb function outcomes [13,14,16,18-20,22,27], with the results presented in **Fig. 4**. There was no significant difference in upper limb

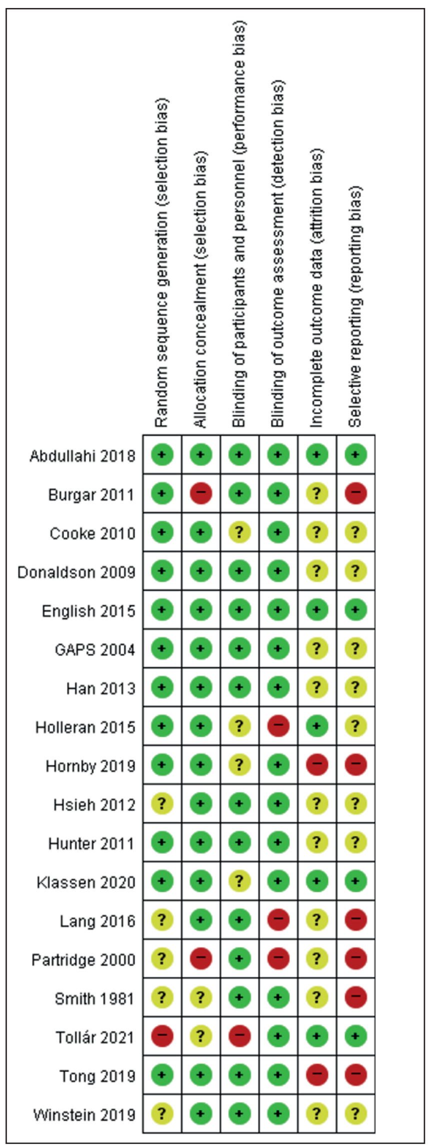

Fig. 2. Risk of bias summary for all included studies.

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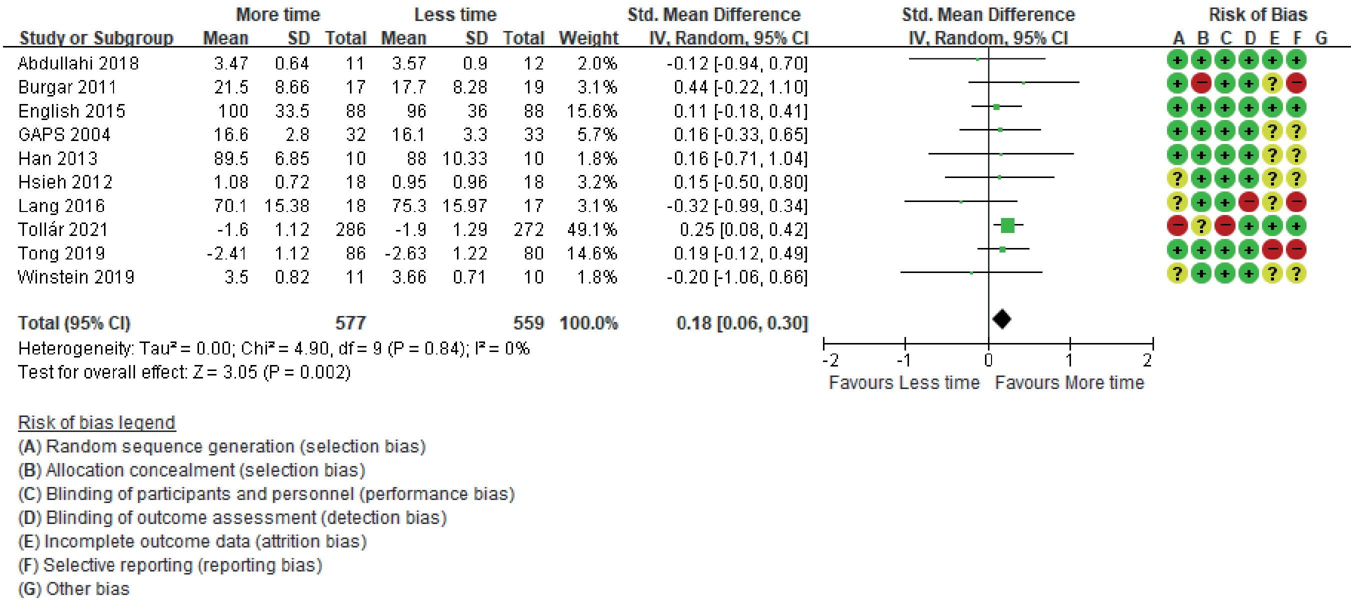


Fig. 3. Forest plot and risk of bias for activities of daily living as an outcome.
SD, standard deviation; IV, inverse-variance; CI, confidence interval.

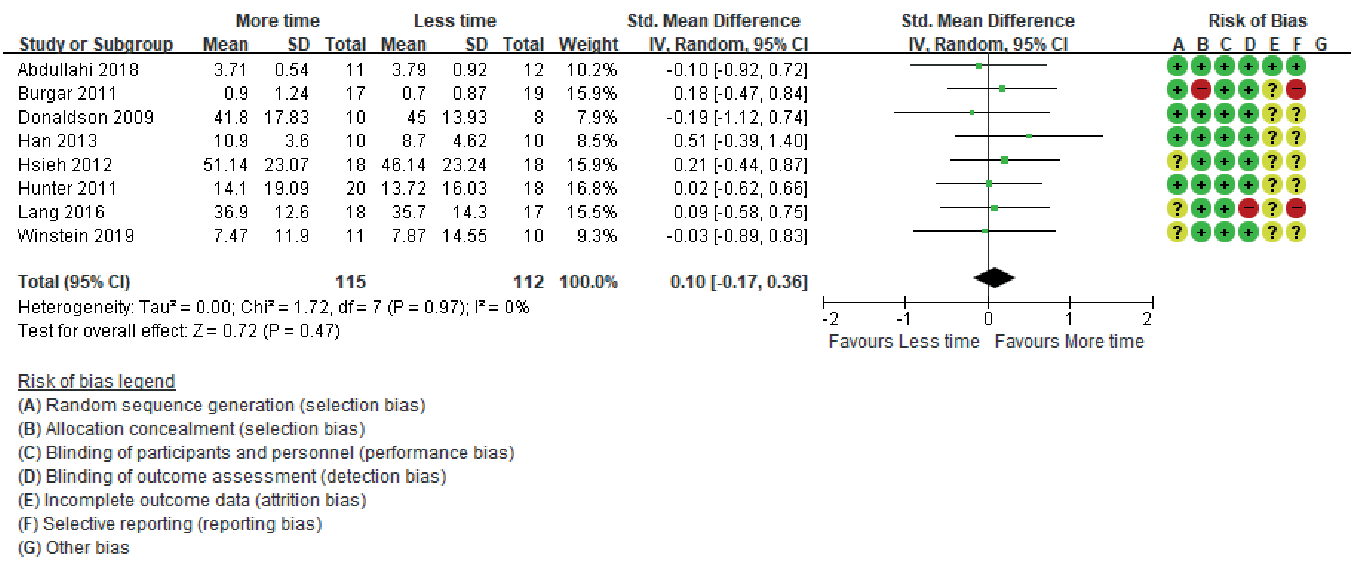


Fig. 4. Forest plot and risk of bias for upper limb function as an outcome.
SD, standard deviation; IV, inverse-variance; CI, confidence interval.

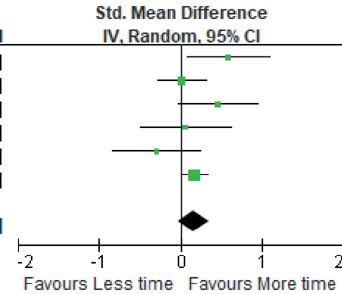
function between the "more time" and "less time" exercise therapy groups (SMD, 0.10; 95% CI, −0.17, 0.36; p = 0.47).

Lower limb function

For lower limb function outcomes, we analyzed six RCTs and presented the results in **Fig. 5** [12,15,17,21,23,25]. No significant difference was observed in lower limb function between the "more time" and "less time" exercise therapy groups (SMD, 0.16; 95% CI, −0.03, 0.35; p = 0.10). Two RCTs comparing the higher-intensity and lower-intensity groups used lower limb function as an outcome measure [28,29]. As shown in **Fig. 6**, higher-intensity exercise

Study or Subgroup	More time Mean	More time SD	More time Total	Less time Mean	Less time SD	Less time Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Cooke 2010	0.55	0.49	32	0.3	0.35	31	11.0%	0.58 [0.07, 1.08]	+	+	?	+	?	?	
English 2015	108	145	88	105.5	197.5	88	22.5%	0.01 [-0.28, 0.31]	+	+	+	+	+	+	
GAPS 2004	9.7	3.3	32	8.1	3.6	34	11.6%	0.46 [-0.03, 0.95]	+	+	+	+	?	?	
Klassen 2020	315	142	24	307	118	25	9.3%	0.06 [-0.50, 0.62]	+	+	−	+	+	+	
Partridge 2000	-49.2	32	33	-39.9	29.9	22	9.8%	-0.29 [-0.84, 0.25]	?	−	+	−	?	−	
Tollár 2021	308.2	103.29	286	290.8	99.14	272	35.8%	0.17 [0.01, 0.34]	+	+	−	+	?	?	
Total (95% CI)			**495**			**472**	**100.0%**	**0.16 [-0.03, 0.35]**							

Heterogeneity: Tau² = 0.02; Chi² = 7.82, df = 5 (P = 0.17); I² = 36%
Test for overall effect: Z = 1.63 (P = 0.10)

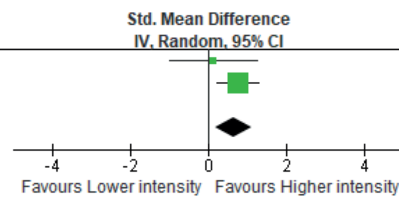


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Fig. 5. Forest plot and risk of bias for lower limb function as an outcome.
SD, standard deviation; IV, inverse-variance; CI, confidence interval.

Study or Subgroup	Higher intensity Mean	Higher intensity SD	Higher intensity Total	Lower intensity Mean	Lower intensity SD	Lower intensity Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Holleran 2015	231	121	6	213	125	6	17.8%	0.14 [-1.00, 1.27]	+	?	?	−	+	?	
Hornby 2019	294	95.87	28	231	64.84	32	82.2%	0.77 [0.24, 1.30]	+	+	+	+	+	+	
Total (95% CI)			**34**			**38**	**100.0%**	**0.66 [0.18, 1.13]**							

Heterogeneity: Tau² = 0.00; Chi² = 0.99, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 2.70 (P = 0.007)

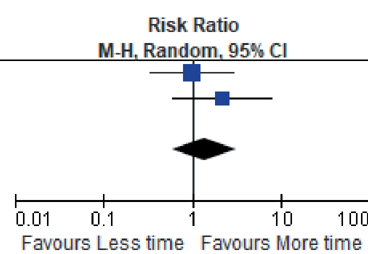


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Fig. 6. Forest plot and risk of bias for lower limb function as an outcome.
SD, standard deviation; IV, inverse-variance; CI, confidence interval.

Study or Subgroup	More time Events	More time Total	Less time Events	Less time Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
English 2015	6	96	6	94	58.0%	0.98 [0.33, 2.93]	+	+	+	+	+	+	
Smith 1981	7	46	3	43	42.0%	2.18 [0.60, 7.90]	?	?	+	+	?	−	
Total (95% CI)		**142**		**137**	**100.0%**	**1.37 [0.60, 3.16]**							
Total events	13		9										

Heterogeneity: Tau² = 0.00; Chi² = 0.86, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 0.74 (P = 0.46)



Risk of bias legend
(A) Random sequence generation (selection bias)
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(C) Blinding of participants and personnel (performance bias)
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(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Fig. 7. Forest plot and risk of bias for adverse events.
M-H, Mantel-Haenszel; CI, confidence interval.

Table 1. Evidence summary

Amount	Outcomes	Importance	Number of participants (studies)	Certainty of evidence (GRADE)	Statistical method	Effect size
Time	Activities of daily living	7	1,136 (10)	Moderate	SMD (IV, random, 95% CI)	0.18 (0.06, 0.30)
Time	Upper limb function	6	227 (8)	Low	SMD (IV, random, 95% CI)	0.10 (−0.17, 0.36)
Time	Lower limb function	8	967 (6)	Moderate	SMD (IV, random, 95% CI)	0.16 (−0.03, 0.35)
Intensity	Lower limb function	8	72 (2)	Low	SMD (IV, random, 95% CI)	0.66 (0.18, 1.13)
Time	Adverse events	6	279 (2)	Very low	RR (M-H, random, 95% CI)	1.37 (0.60, 3.16)

GRADE, Grading of Recommendations Assessment, Development and Evaluation; SMD, standardized mean difference; IV, inverse-variance; CI, confidence interval; RR, risk ratio; M-H, Mantel-Haenszel.

therapy significantly improved lower limb function compared to lower-intensity exercise therapy (SMD, 0.66; 95% CI, 0.18, 1.13; p = 0.007).

Adverse events

As presented in **Fig. 7**, two studies compared serious adverse events [17,24], with no significant differences found in the meta-analysis (RR, 1.37; 95% CI, 0.60, 3.16; p = 0.46). The adverse events monitored in these studies included death, stroke recurrence, and falls.

Certainty of evidence

Using the GRADE system, the evidence was rated as moderate for activities of daily living, low for upper limb function, moderate (time) and low (intensity) for lower limb function, and very low for adverse events. No serious risk of bias, inconsistency, indirectness, or publication bias was observed, but the small number of participants for adverse events led to a very low evidence level.

Recommendation

The results of meta-analyses and the evidence level for each outcome are summarized in **Table 1**. Based on these findings, the recommendation for the key question is as follows: "In stroke patients, to enhance activities of daily living and motor function, the total amount of upper and lower limb exercise therapy may be increased, taking into account the patient's neurological and medical status." The recommendation grade is "conditional recommend," with a "low" level of evidence.

DISCUSSION

Our meta-analyses have shown that increasing the total amount (time) of exercise therapy can lead to significant improvements in activities of daily living. Similarly, augmenting the intensity of exercise therapy can significantly improve lower limb function. Additionally, increasing the total amount of exercise therapy did not lead to an increase in adverse events. Therefore, it is feasible to augment the total amount of exercise therapy, tailored to the patient's condition, to improve daily living activities and motor functions in stroke patients. Based on the findings of our meta-analysis and expert opinions from the field of rehabilitation, we recommend that physicians consider increasing the total amount of exercise therapy for stroke patients to improve activities of daily living and motor function, taking into account the patients' neurological and medical conditions. However, due to the small sample sizes in most studies, larger-scale RCTs are necessary to provide stronger evidence.

The present study provides evidence supporting an increase in the total amount of exercise therapy for stroke patients. Rehabilitation specialists can extend the total exercise time to improve activities of daily living and intensify the exercise to enhance lower limb function in these patients. However, concerns about potential adverse effects remain due to the lack of evidence regarding the safety of higher-intensity exercise therapy. Given the high prevalence of comorbid conditions such as cardiovascular disease and diabetes among stroke patients, individualized approaches are essential. Currently, there is no standard measure for the absolute amount of total exercise therapy due to variations in therapy protocols and patient characteristics among individuals with stroke. Additionally, it was not possible to compare the total amount of exercise therapy across studies involving different types of exercise. Therefore, our meta-analysis only included studies that varied the total amount of the same type of exercise. To establish stronger evidence, large-scale RCTs that precisely define and compare the total amount (frequency, intensity, and duration) of exercise therapy are necessary. Furthermore, a methodology to compare the total amount of different types of exercise therapy should be developed.

Facilitators for increasing the total amount of exercise therapy include the willingness of patients and caregivers to engage in intensive therapy. Patients who have experienced a stroke and their caregivers often seek more extensive exercise therapy to achieve better functional recovery and minimize impairments and disabilities. The primary barrier to increasing the total amount of exercise therapy is the absence of standard guidelines and a lack of sufficient evidence regarding safety. Additionally, patients may not be fully aware of the potential adverse effects that can arise from increasing the amount of exercise therapy, especially due to the unclear standards for determining optimal amounts. Therefore, it is necessary to carefully weigh the medical benefits against the risks of adverse events on an individual basis. Community-based exercise programs or group therapies may be advantageous for neurologically and medically stable patients who have a low cardiovascular risk.

To increase the total amount of exercise therapy, the most preferred method involves extending the frequency or duration of exercise therapy sessions. However, this approach necessitates additional therapy personnel, enhanced rehabilitation facilities, and increased insurance coverage support, leading to substantial costs. Consequently, alternative strategies are essential to augment exercise therapy without significantly escalating healthcare expenses. For instance, the exercise obtained solely through individual rehabilitation sessions with a physical therapist might be both insufficient and costly. Therefore, it is crucial to explore and assess various options, such as creating exercise education programs that stroke patients can independently follow or encouraging group rehabilitation activities in community settings outside of hospitals.

The limitations of this study should be acknowledged. Given the scarcity of research analyzing the individual effects of frequency and duration, our analysis focused on the total time spent in exercise therapy, as determined by frequency and duration. Among the included studies, only two evaluated the effects of intensity, and none assessed the potential adverse effects of increasing exercise intensity. Due to the limited number of RCTs examining the impact of exercise therapy on clinical outcomes, we cannot provide strong evidence. Additionally, the small sample sizes in most studies hinder the generalizability of the findings to the broader population. Although we conducted a meta-analysis on the effects of exercise therapy, the lack of a standardized exercise protocol, coupled with methodological variations across studies, precludes recommending an optimal total amount of exercise therapy based solely on our results. Furthermore, while neurological status changes over time post-stroke, the number of studies is insufficient to conduct separate meta-analyses for acute, subacute, and chronic stages. Future research should include large-scale RCTs to examine the effects of frequency, duration, intensity, and type of exercise, as well as their specific combinations across various post-stroke stages.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Search terms and strategies

Supplementary Table 2

Characteristics of included studies

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