

Effects of different rehabilitation therapies on upper extremity motor function and activities of daily living in hemiplegic patients with stroke

A network meta-analysis

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Abstract

Background: To compare the effects of different rehabilitation therapies on the scores of Fugl-Meyer assessment of motor recovery (FMA), the action research arm test (ARAT), and modified Barthel index in hemiplegic patients with stroke by a network meta-analysis.

Methods: We searched Embase, PubMed, Web of Science, and Cochrane Library from their inception until April 1, 2024 for randomized controlled trials (RCTs) on the effects of rehabilitation therapies on upper extremity motor function and activities of daily living in hemiplegic patients with stroke. Data analyses were conducted using R software.

Results: Seventeen RCTs were included, involving 901 patients and 10 rehabilitation therapies. The network meta-analysis revealed that mirror therapy (mean difference [MD] = 4.94, 95% confidence interval [CI]: 4.3–5.59, $P < .05$), neuromuscular electrical stimulation (NMES) + robotic therapy (RT) (MD = 7.1, 95% CI: 3.15–11.10, $P < .05$), RT (MD = 4.7, 95% CI: 0.98–8.41, $P < .05$), and transcranial direct current stimulation (MD = –4.92, 95% CI: –6.12 to –3.72, $P < .05$) outperformed conventional therapies in the improvement of FMA. NMES + RT (MD = 4.6, 95% CI: 0.42–8.76, $P < .05$) and repetitive facilitative exercise (RFE) + botulinum toxin type A (BoNT-A) (MD = 8, 95% CI: 4.43–11.52, $P < .05$) outperformed conventional therapies in the improvement of ARAT. Action observation (AO) (MD = 6, 95% CI: 0.11–11.85, $P < .05$) was superior to conventional therapies in the improvement of activities of daily living. RFE + BoNT-A had the highest surface under the cumulative ranking curve value for FMA improvement and ARAT improvement. The surface under the cumulative ranking curve value for modified Barthel index improvement was the highest for AO.

Conclusion: RFE + BoNT-A and AO exhibit advantages in improving upper extremity motor function and AO, respectively. Due to some limitations in this study, more high-quality RCTs are still required to validate our findings.

Abbreviations: ADL = activities of daily living, AO = action observation, ARAT = action research arm test, BoNT-A = botulinum toxin type A, CIs = confidence intervals, DIC = deviance information criterion, FES = functional electrical stimulation, FMA = Fugl-Meyer assessment of motor recovery, FMS = functional magnetic stimulation, MBI = modified Barthel index, MD = mean difference, MT = mirror therapy, NMA = network meta-analysis, NMES = neuromuscular electrical stimulation, RCTs = randomized controlled trials, RFE = repetitive facilitative exercise, RT = robotic therapy, rTMS = repetitive transcranial magnetic stimulation, ST = sham treatment, SUCRA = surface under the cumulative ranking curve, tDCS = transcranial direct current stimulation, UEMF = upper extremity motor function.

Keywords: activities of daily living, motor function, network meta-analysis, rehabilitation therapy, stroke

HX and LS contributed to this article equally.

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Table 1
Basic study characteristics.

Study	Country	Sample size	Mean age	Gender (M/F)	Intervention	Duration of intervention			Outcome
						Duration	Weekly frequency	Period	
Alisar 2020 ^[19]	Turkey	16/16	63.56/63.5	13/19	tDCS/ST	60–120 min	5	3w	FMA, FIM
Gong 2023 ^[20]	China	37/35	56.3/56.8	57/15	tDCS/ST	2 h	5	4w	FMA
Chan 2009 ^[21]	China	10/10	46/45	11/9	FES/ST	1.5 h	5	3w	FMA, GS, MAS
Fu 2017 ^[22]	China	28/25	62.04/59.76	22/31	AO/ST	20 min	7	4w	FMA, WMFT, MBI
Hokazono 2022 ^[23]	Japan	20/20	60.5/66	25/15	RFE + BoNT-A/ST	40 min	6	4w	FMA, ARAT, MAS
Hu 2015 ^[24]	China	11/15	45.6/49.2	18/9	NMES-RT/ST	60 min	6	7w	FMA, ARAT, MAS
Noh 2019 ^[25]	India	11/11	66.45/57.45	10/12	rTMS + AO/rTMS	1 h	14	5w	FMA
Chang 2022 ^[26]	China	36/15	56.9/61.4	34/17	rTMS/ST	60 min	5	2w	FMA, GS, WMFT
Chen 2020 ^[27]	China	19/16	52.56/48.68	27/8	FMS/rTMS	60 min	7	2w	FMA, BI
Liao 2012 ^[28]	China	10/10	55.51/54.56	13/7	RT/ST	90–105 min	5	4w	FMA, FIM
Ma 2022 ^[29]	China	10/9	59.00/56.44	14/5	RT/ST	90 min	5	4w	FMA, ARAT, STEF
Lee 2018 ^[30]	Korea	15/15	52.07/50.27	19/11	RT/ST	30 min	5	8w	FMA, MBI
Yuan 2023 ^[31]	China	47/23	57.80/58.90	61/9	RT/ST	60 min	3	3w	FMA, MBI
Chen 2021 ^[32]	China	10/10	47.10/54.90	17/3	RT/ST	30 min	5	2w	FMA, ARAT, MBI
Zhang 2023 ^[33]	China	152/152	57.46/57.71	157/147	MT/ST	30 min	7	3w	FMA
Wen 2022 ^[34]	China	25/27	53.76/57.78	41/11	MT/ST	30 min	6	3w	FMA, ARAT
Antonioti 2019 ^[35]	Italy	16/19	68.2/69.5	26/14	MT/ST	30 min	5	30d	FMA, FIM, ARAT

AO = action observation, ARAT = action research arm test, BoNT-A = botulinum toxin type A, d = day, FES = functional electrical stimulation, FIM = functional-independence measure, FMA = Fugl-Meyer assessment, FMS = functional magnetic stimulation, GS = grip strength, h = hour, MAS = modified Ashworth Scale, MBI = modified Barthel index, min = minute, MT = mirror therapy, NMES = neuromuscular electrical stimulation, RFE = repetitive facilitative exercise, RT = robot-assisted therapy, rTMS = repetitive transcranial magnetic stimulation, ST = sham treatment, tDCS = transcranial direct current stimulation, w = week, WMFT = wolf motor function test.

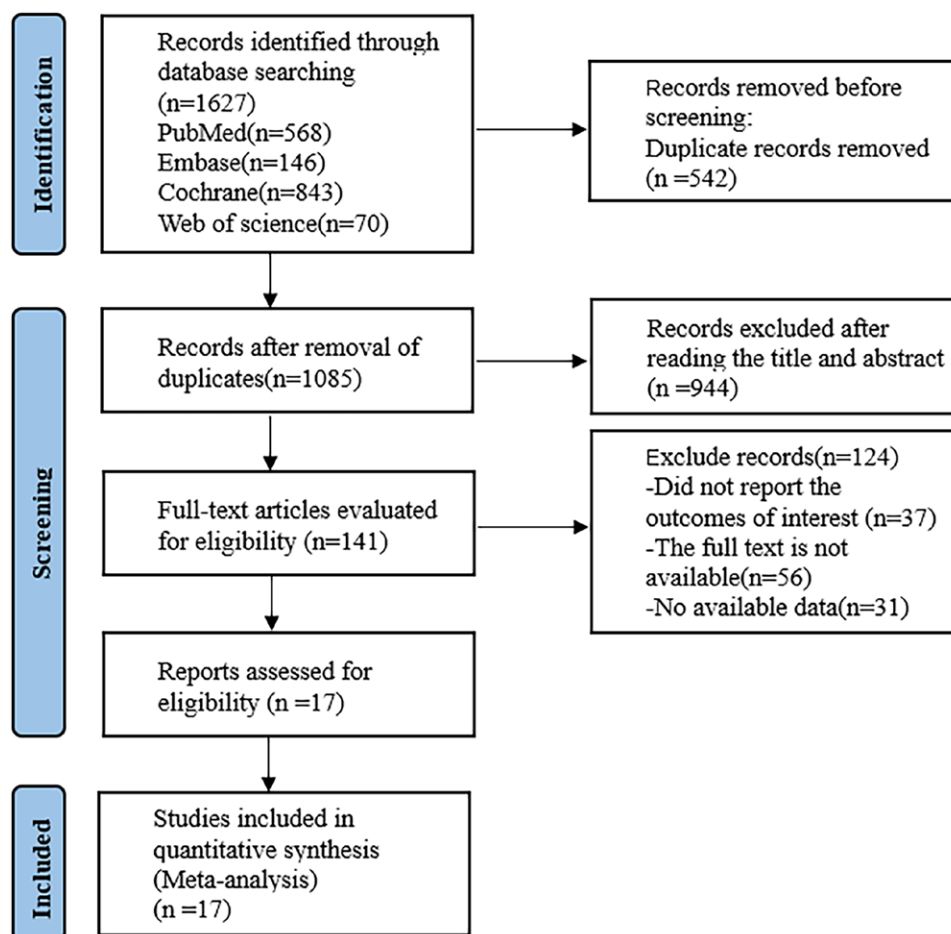


Figure 1. PRISMA flowchart for study selection. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

1. Introduction

Stroke, also known as cerebrovascular accident, is an acute or focal cerebral dysfunction resulting from various vascular etiologies,

including hemorrhage and ischemia, and it can persist over 24 hours.^[1] Characterized by high morbidity, mortality, and disability rates, stroke primarily presents with postural control anomaly,

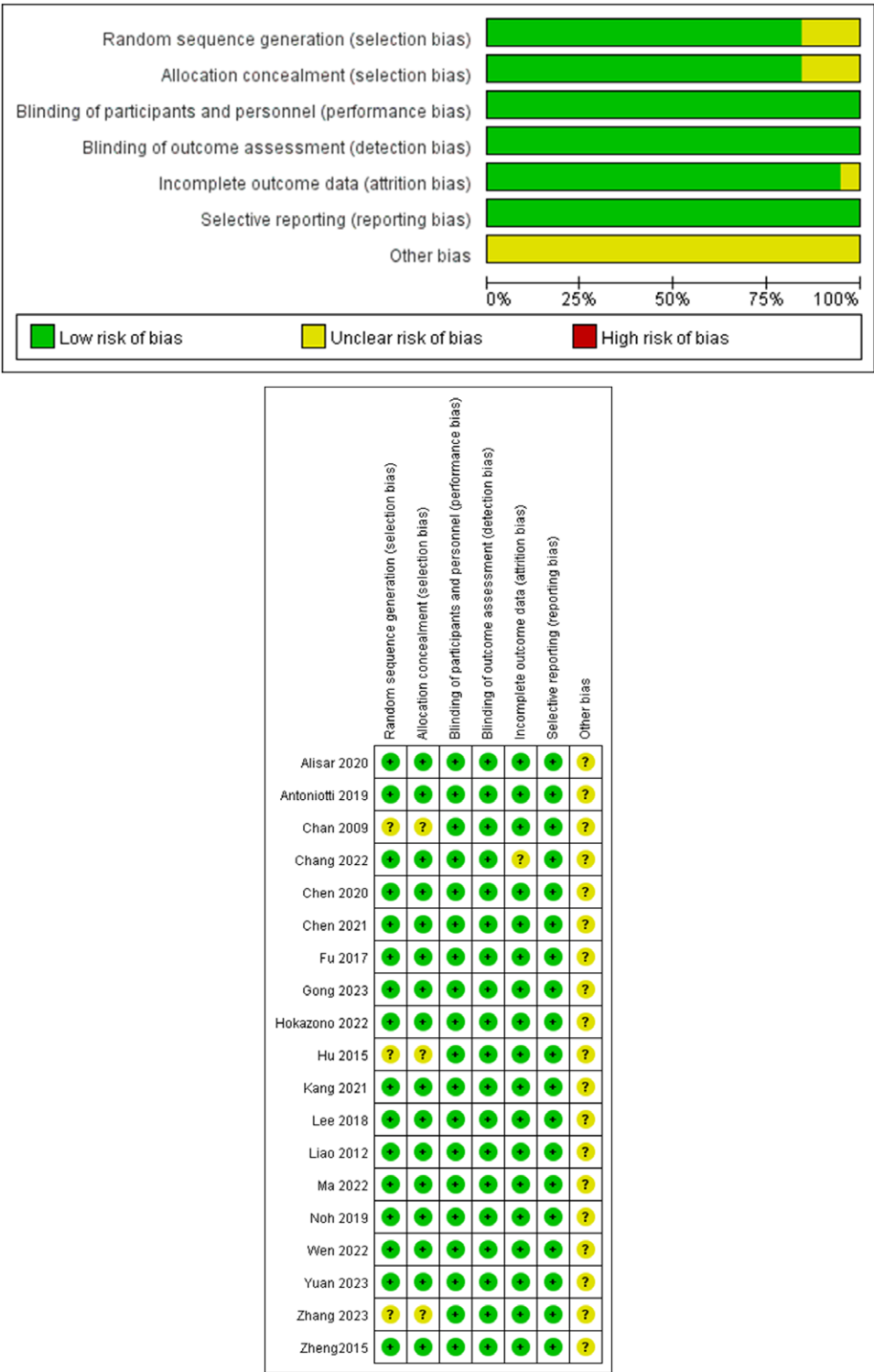


Figure 2. Risk of bias diagram.

abnormal muscular tone and strength, and decline in balance function. As revealed by the stroke survey report of the National Health Commission, stroke is the leading cause of death and disability in Chinese adults, ranking first in the lifetime risk (39.3%) globally.^[2] Post-stroke limb dysfunction, dominated by upper extremity dysfunction, affects 70% to 80% of patients, which imposes a serious impact on the patient's motor function and activities of daily living (ADL) due to delayed recovery, lowering the quality of life, and burdening families and society.^[3] Nowadays, rehabilitation

therapies have been globally recognized as the most effective way to reduce disability in stroke, which perform well in ameliorating limb dysfunction and accelerating rehabilitation. Currently, most stroke patients undergo conventional rehabilitation therapies, but they will be easily fatigued with the training of a single pattern. The Chinese Stroke Rehabilitation Guideline (2020) states that goal-oriented training can increase the intensity of exercise, and underscores the effectiveness of device-aided exercise rehabilitation training in improving limb function in stroke patients.^[4]

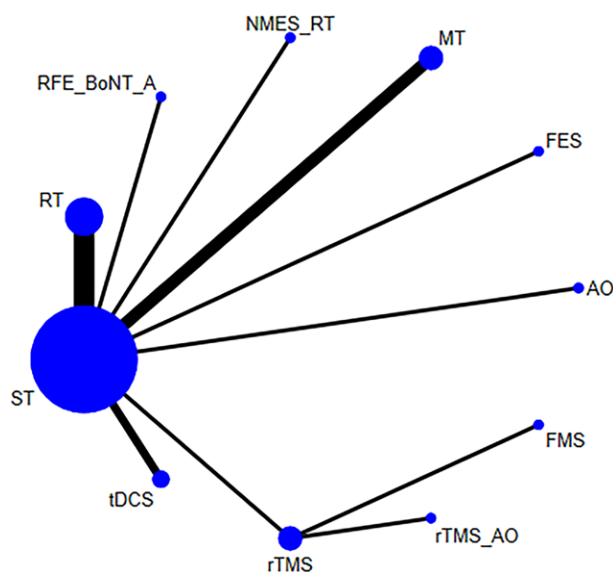


Figure 3. Network diagram for FMA. AO = action observation, FMA = Fugl-Meyer assessment of motor recovery, FMS = functional magnetic stimulation, NMES = neuromuscular electrical stimulation.

As science and technology advance recently, rehabilitation therapies (including exercise therapy, occupational therapy, and physical therapy) for upper extremity hemiplegia in stroke have been emerging, and different therapies and their intervention effects have been investigated globally. In Japan, electrical stimulation therapy is recommended for rehabilitation of upper extremity motor function (UEMF) in stroke patients.^[5] Ada et al.^[6] found that mandatory exercise therapy, motor imagery therapy, and virtual reality are effective in improving UEMF. Marangolo et al.^[7] argued that transcranial direct current stimulation (tDCS) can effectively ameliorate upper extremity motor dysfunction in stroke patients. Mekbib and Takebayashi et al.^[8,9] confirmed that robotic therapy (RT) and mirror therapy (MT) are superior to conventional rehabilitation therapies in enhancing limb mobility and ADL in stroke patients. Increasingly more high-quality systematic reviews and meta-analyses have recently revealed that low- and moderate-intensity exercise therapy can significantly contribute to the rehabilitation of physical function and improvement of health-related quality of life in the elderly, and exercise-based interventions have been widely endorsed by evidence-based medical guidelines.^[10–12] However, no definitive conclusion has been reached. In previous studies, each intervention was compared with the control (sham and conventional physical therapy), but the comparison of different interventions is still lacking. Network meta-analysis (NMA) enables direct or indirect comparison of multiple interventions.^[13] Therefore, this NMA was conducted to assess and rank the effectiveness of different rehabilitation therapies for ameliorating UEMF and ADL in hemiplegic patients with stroke, thereby offering an evidence-based basis for selecting optimal rehabilitation interventions in clinical practice.

2. Materials and methods

2.1. Registration

The study protocol was registered with PROSPERO (CRD42024552390).

2.2. Eligibility criteria

Inclusion criteria: study design: randomized controlled trials (RCTs); population: patients diagnosed with stroke, accompanied

Table 2
League table for FMA.

MD 95% CI	
FES	
FMS	
1.9 (-9.3, 13.16)	
0.64 (-7.51, 8.81)	
-0.24 (-10.56, 7.54)	
-3.88 (-18.22, 10.27)	
0.9 (-8.05, 9.84)	
4.69 (-4.19, 13.63)	
4.21 (-15.39, 23.83)	
6.84 (-4.33, 18.09)	
1.91 (-9.32, 13.23)	
0.68 (-7.53, 8.91)	
MT	
-2.15 (-6.12, 1.85)	
-4.55 (-16.27, 7.09)	
0.24 (-3.52, 4.01)	
2.81 (-4.06, 9.62)	
2.27 (-16.45, 21.02)	
4.94 (4.3, 5.59)*	
0.03 (-1.33, 1.39)	
NMES + RT	
-2.39 (-14.74, 9.86)	
2.4 (-2.98, 7.79)	
4.95 (-2.96, 12.78)	
4.42 (-14.61, 23.51)	
7.1 (3.15, 11.01)*	
2.18 (-1.95, 6.27)	
RFE + BoNT-A	
4.79 (-7.39, 17.05)	
7.33 (-6.13, 20.88)	
6.82 (-15.13, 28.81)	
9.49 (-2.12, 21.2)	
2.57 (-5.21, 10.31)	
2.04 (-16.99, 21.15)	
4.7 (0.98, 8.41)*	
-0.22 (-4.13, 3.68)	
4.57 (-7.08, 16.34)	
2.18 (-1.95, 6.27)	
0.03 (-1.33, 1.39)	
1.91 (-9.32, 13.23)	
0.68 (-7.53, 8.91)	
RT	
2.57 (-5.21, 10.31)	
2.04 (-16.99, 21.15)	
4.7 (0.98, 8.41)*	
-0.53 (-17.9, 16.92)	
2.13 (-4.66, 8.98)	
-2.79 (-9.68, 4.16)	
-0.22 (-4.13, 3.68)	
4.57 (-7.08, 16.34)	
2.18 (-1.95, 6.27)	
0.03 (-1.33, 1.39)	
1.91 (-9.32, 13.23)	
0.68 (-7.53, 8.91)	
rTMS	
-0.53 (-17.9, 16.92)	
2.13 (-4.66, 8.98)	
-2.79 (-9.68, 4.16)	
-0.22 (-4.13, 3.68)	
4.57 (-7.08, 16.34)	
2.18 (-1.95, 6.27)	
0.03 (-1.33, 1.39)	
1.91 (-9.32, 13.23)	
0.68 (-7.53, 8.91)	
rTMS + AO	
2.68 (-16.09, 21.38)	
-2.24 (-21.03, 16.51)	
-4.92 (-6.12, -3.72)*	
ST	
-4.92 (-6.12, -3.72)*	

CI = confidence interval, FMA = Fugl-Meyer assessment, MD = mean difference.

*means $P < .05$.

Table 3
SUCRA rank.

Treatment	FMUE (%)	ARAT (%)	MBI (%)
AO	54.8		91.1
FES	55.7		
FMS	63.1		
MT	50.7	35.1	
NMES + RT	72.4	61.3	
RFE + BoNT-A	75.7	91.7	
RT	48.5	49.4	47.9
rTMS	28.1		
rTMS + AO	40.8		
ST	9.8	12.6	11.0
tDCS	50.3		

AO = action observation, ARAT = action research arm test, BoNT-A = botulinum toxin type A, FES = functional electrical stimulation, FMA = Fugl-Meyer assessment, FMS = functional magnetic stimulation, MBI = modified Barthel index, MT = mirror therapy, NMES = neuromuscular electrical stimulation, RFE = repetitive facilitative exercise, RT = robot-assisted therapy, rTMS = repetitive transcranial magnetic stimulation, ST = sham treatment, tDCS = transcranial direct current stimulation.

by upper extremity dysfunction; interventions: tDCS, functional electrical stimulation (FES), functional magnetic stimulation (FMS), action observation (AO), repetitive facilitative exercise combined with botulinum toxin type A (RFE + BoNT-A), RT, repetitive transcranial magnetic stimulation (rTMS), neuromuscular electrical stimulation (NMES), MT, and rTMS + AO in the test group, and conventional rehabilitation therapies in the control group; and outcomes: Fugl-Meyer assessment of motor recovery-upper extremity (FMA), the action research arm test (ARAT), and modified Barthel index (MBI). Exclusion criteria: the values of outcome metrics could not be converted and obtained from the original authors; non-English studies; studies of poor quality; and duplicate publications.

2.3. Search strategy

We systematically searched Embase, PubMed, Web of Science, and Cochrane Library from their inception until April 1, 2024. The search term was composed of subject words and free words, including “stroke/cerebral stroke/apoplexy/cerebral infarction/cerebral hemorrhage/cerebrovascular accident,” “constraint-induced movement therapy/ CIMT/virtual reality/virtual environment/robot,” “Hemiplegia/Transient/Post-Ictal Crossed,” and “randomized controlled trial/random.” The search process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The search strategy is detailed in File S1, Supplemental Digital Content, <https://links.lww.com/MD/Q541>.

2.4. Screening and data extraction

Two reviewers with 3 or more years of relevant experience in stroke nursing were independently responsible for study screening and data extraction. After duplicates were eliminated by EndNote X9, the following key data were extracted: first author, year of publication, country, sample size, gender, age, interventions, duration of intervention, and primary outcomes. Discrepancies, if any, were settled by discussion or consultation with a third reviewer with 10 or more years of relevant experience. All 3 reviewers were trained regarding evidence-based medicine and evidence-based nursing.

2.5. Quality assessment

Two reviewers (A and B) independently assessed the quality of the included studies using the Cochrane Risk of Bias Tool 2.0. Each study was rated as “low risk,” “high risk,” or “some

concerns” across the 6 domains: randomization, allocation concealment, blinding, incomplete data, selective reporting, and others. The overall quality was considered grade A if all domains were rated as “low risk,” grade B if at least one domain was rated as “some concerns” without “high risk,” and grade C if one domain was rated as “high risk.” Discrepancies, if any, were settled by discussion or consultation with a third reviewer with 10 or more years of relevant experience.

2.6. Statistical analysis

The included studies were assessed for risk of bias using Review Manager 5.4, and NMA was conducted using R Foundation for Statistical Computing, with non-informative prior Bayesian NMA performed in R “BUGSnet”^[14] and “gemtc”^[15] packages with specific parameters (100,000 simulation iterations and 10,000 adaptive iterations). Each result underwent Markov chain Monte Carlo simulations, with a refinement interval of 10 (one sample was collected every 10 iterations). Model convergence was assessed using trace and density plots, and quantified using the Brooks-Gelman-Rubin statistic. Node-splitting method^[16] and posterior distribution plot^[17] were utilized to test local consistency and global consistency, respectively. A fixed-effects model was adopted when no significant heterogeneity was found ($P > .1$, $I^2 < 50\%$); otherwise, a random-effects model was adopted ($P \leq .1$, $I^2 \geq 50\%$). All outcome metrics were continuous data, so the mean difference (MD) was used as the effect size measure for them, with 95% confidence intervals (CIs) calculated. The surface under the cumulative ranking curve (SUCRA) value was calculated to rank the probability of being the best intervention, and the higher the SUCRA value, the better the effect. The significance level was set at .05. Finally, a comparison-adjusted funnel plot was generated by STATA 15.0^[18] (Stata Corporation, College Station) to assess publication bias.

3. Results

3.1. Search results

Initially, 1627 relevant studies were retrieved, of which duplicates were excluded. Following title and abstract reviews, the full text of the remaining 121 potentially relevant studies was read. Finally, 17 RCTs were included (Fig. 1).

3.2. Basic study characteristics and quality assessment results

3.2.1. Basic study characteristics. The included studies were carried out in 6 countries. A total of 901 patients were involved, and they underwent 10 rehabilitation therapies: tDCS, FES, FMS, AO, RFE + BoNT-A, RT, rTMS, NMES, MT, and rTMS + AO. The intervention effect was assessed by FMA, ARAT, and MBI scores. The basic study characteristics are shown in Table 1.

3.2.2. Quality assessment results. All the included studies were double-arm trials. The specific randomization methods were described in 14 studies, and the allocation concealment methods (opaque envelopes and computer-generated random numbers) were described in 14 studies. Four studies used double-blind methods, 8 used single-blind methods, and the rest did not specify whether blinding was implemented. Sixteen studies had complete data, and 17 had no selective reporting. The quality of all studies was considered grade B (Fig. 2).

3.3. Results of NMA

3.3.1. Results of NMA for FMA. The FMA was reported as an outcome in 17 studies,^[19–35] involving ten rehabilitation

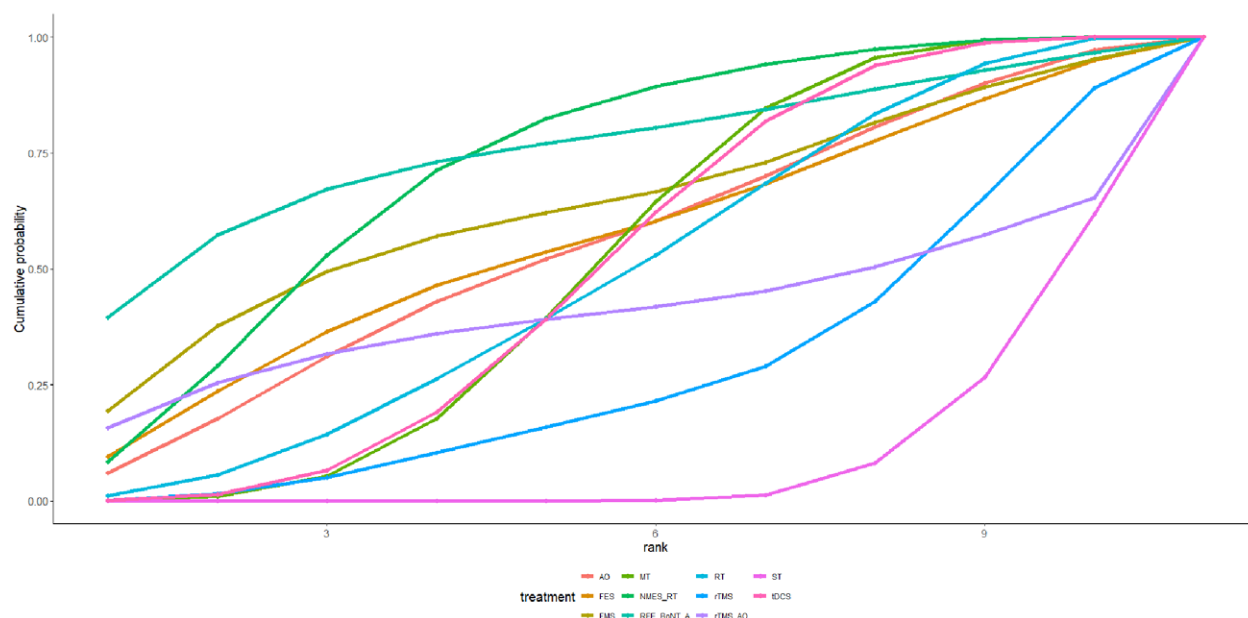


Figure 4. Cumulative probability diagram for FMA. AO = action observation, FMA = Fugl-Meyer assessment of motor recovery, FMS = functional magnetic stimulation, NMES = neuromuscular electrical stimulation.

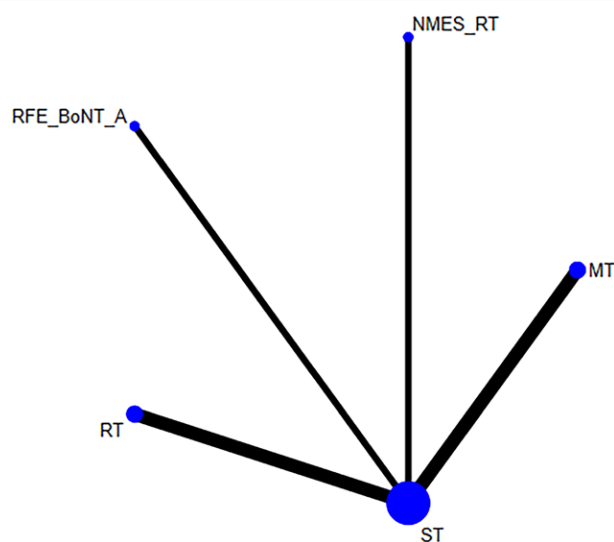


Figure 5. Network diagram for ARAT. ARAT = action research arm test.

therapies. In the network diagram (Fig. 3), no closed loop was formed. Consistency modeling was conducted on the overall data, and a fixed-effects model was adopted ($I^2 < 50\%$). In the inconsistency test, the difference in deviance information criterion (DIC) was < 5 ($P > .05$), suggesting better overall consistency. Therefore, a consistency model was adopted. The results revealed that MT (MD = 4.94, 95% CI: 4.3–5.59, $P < .05$), NMES + RT (MD = 7.1, 95% CI: 3.15–11.10, $P < .05$), and RT (MD = 4.7, 95% CI: 0.98–8.41, $P < .05$) performed better in ameliorating upper extremity dysfunction than conventional therapies, and RFE + BoNT-A was superior to NMES + RT, FMS, AO, MT, tDCS, RT, rTMS + AO, and rTMS (Table 2). Besides, RFE + BoNT-A had the highest SUCRA value (75.7%) for FMA improvement, followed by NMES + RT (72.4%), FMS (63.1%), and rTMS (28.1%) (Fig. 4, Table 3).

3.3.2. Results of NMA for ARAT. ARAT was reported as an outcome in 6 studies,^[23,24,29,32,34,35] involving four rehabilitation therapies. In the network diagram (Fig. 5), no closed loop was

formed. Consistency modeling was conducted on the overall data, and a fixed-effects model was adopted ($I^2 < 50\%$). In the inconsistency test, the difference in DIC was < 5 ($P > .05$), suggesting better overall consistency. Therefore, a consistency model was adopted. The results revealed that NMES + RT (MD = 4.6, 95% CI: 0.42–8.76, $P < .05$) and RFE + BoNT-A (MD = 8, 95% CI: 4.43–11.52, $P < .05$) performed better in ameliorating upper extremity dysfunction than conventional therapies, and RFE + BoNT-A was superior to NMES + RT, FMS, AO, MT, tDCS, RT, rTMS + AO, and rTMS (Table 4). Besides, RFE + BoNT-A had the highest SUCRA value (91.7%) for ARAT improvement, followed by NMES + RT (61.3%), RT (49.4%), and MT (35.1%) (Fig. 6, Table 3).

3.3.3. Results of NMA for MBI. Four studies^[22,30–32] reported MBI as an outcome, involving 2 rehabilitation therapies. In the network diagram (Fig. 7), no closed loop was formed. Consistency modeling was conducted on the overall data, and a fixed-effects model was adopted ($I^2 < 50\%$). In the inconsistency test, the difference in DIC was < 5 ($P > .05$), suggesting better overall consistency. Therefore, a consistency model was adopted. The results revealed that AO (MD = 6, 95% CI: 0.11–11.85, $P < .05$) outperformed conventional therapies in enhancing ADL (Table 5). Besides, the SUCRA value for MBI improvement was the highest for AO (91.1%) and lowest for RT (47.9%) (Fig. 8, Table 3).

3.4. Publication bias

The presence or absence of publication bias in the included studies was detected using funnel plots. We observed that the funnel plots for FMA, ARAT, and MBI as outcome metrics had poor symmetry, suggesting possible publication bias or a small sample effect (Fig. 9).

4. Discussion

4.1. Main findings

This Bayesian NMA included 17 RCTs involving 10 rehabilitation therapies to compare the effects of different rehabilitation therapies on UEMF and ADL in hemiplegic patients with stroke,

Table 4
League table for ARAT.

MD 95% CI				
MT				
−2.69 (−10.11, 4.76)	NMES + RT			
−6.09 (−13.12, 1.05)	−3.39 (−8.87, 2.11)	RFE + BoNT-A		
−1.54 (−12.16, 8.96)	1.14 (−8.46, 10.73)	4.51 (−4.81, 13.86)	RT	
1.91 (−4.23, 8.05)	4.6 (0.42, 8.76)*	8 (4.43, 11.52)*	3.47 (−5.17, 12.09)	ST

ARAT = action research arm test, CI = confidence interval, MD = mean difference, MT = mirror therapy.
*Means $P < .05$.

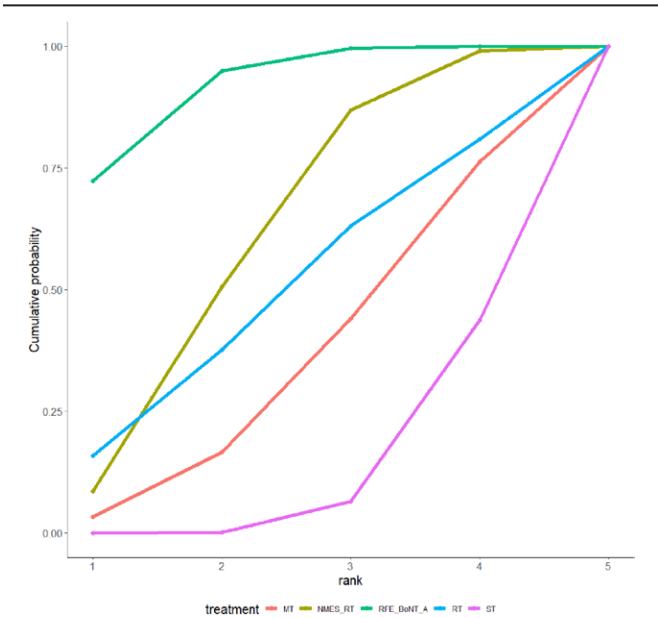


Figure 6. Cumulative probability diagram for ARAT. ARAT = action research arm test.

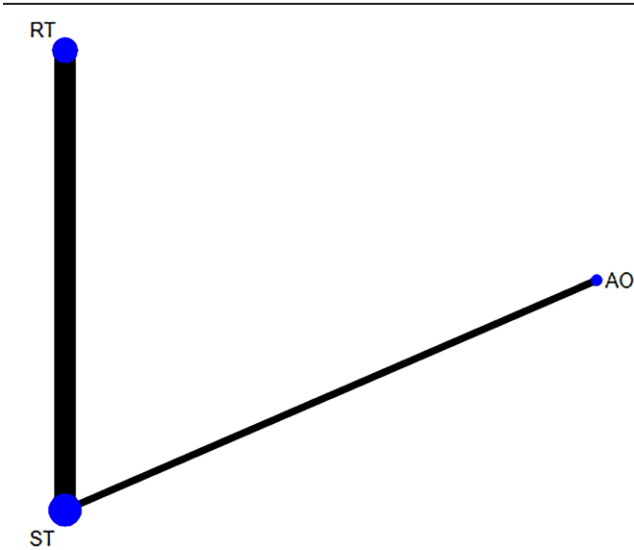


Figure 7. Network diagram for MBI. MBI = modified Barthel index.

with FMA, ARAT, and MBI as the outcome metrics. FMA and ARAT were used for the assessment of UEMF and MBI for ADL. We found that the 10 rehabilitation therapies all outperformed conventional therapies in enhancing both UEMF and ADL. RFE + BoNT-A was identified as the best intervention for

Table 5
League table for MBI.

MD 95% CI		
AO		
3.91 (−3.66, 11.51)	RT	
6 (0.11, 11.85)*	2.08 (−2.74, 6.9)	ST

AO = action observation, CI = confidence interval, MBI = modified Barthel index, MD = mean difference, RT = robot-assisted therapy.
*means $P < .05$.

improving FMA and ARAT, and AO was the most effective in improving MBI in hemiplegic patients with stroke.

4.2. RFE + BoNT-A: Best intervention for improving FMA and ARAT

FMA and ARAT are the most frequently used outcome metrics when assessing UEMF in hemiplegic patients with stroke. FMA generally assesses the status of upper extremity functional recovery from reflex, sensory, and motor functions, whereas ARAT focuses more on the assessment of the fine motor function of the hand and often serves as a secondary outcome measure.^[34] This NMA revealed that 10 rehabilitation therapies (e.g., MT, NMES + RT, RT, tDCS, and RFE + BoNT-A) plus conventional therapies were all effective in ameliorating UEMF in hemiplegic patients with stroke as compared to conventional therapies alone, among which RFE + BoNT-A performed best. RFE has been widely used in rehabilitation training for hemiplegic patients with stroke, which, by reconstructing and reinforcing injured nerve bundles associated with the desired action, helps achieve a desired set of actions. BoNT-A injection can restore muscular tone and increase the passive range of motion, so it has been widely applied to alleviate and control post-stroke focal spasticity.^[36] As recommended in the Japanese Guidelines for the Management of Stroke, RFE should be used as a grade B motor therapy for the affected upper extremity after stroke, but its effect is often restricted when the paralyzed limb develops spasticity.^[37] Wissel et al^[38] found in an RCT that RFE helps improve not only motor dysfunction but also manipulation of objects, effectively ameliorating UEMF in hemiplegic patients with stroke. Ojardias et al^[39] argued that BoNT-A injection can restore muscular tone and raise the passive range of motion. However, whether BoNT-A injection alone can enhance autonomous motor control and upper extremity function in patients with chronic stroke remains unclear. The effect of BoNT-A injection plus adjuvant motor therapy has been investigated in several RCTs, but its capability to improve the affected upper extremity function is rarely reported. Nasb et al^[40] demonstrated that RFE + BoNT-A can enhance motor function and mitigate motor injury in the stroke-associated chronically paralyzed upper extremity with spasticity, which induces highly repetitive voluntary movements to raise the efficiency of sustained motor learning of the affected upper extremity and further effectively ameliorate the UEMF in hemiplegic patients with stroke. In this study, RFE + BoNT-A was implemented in only one included study, leading to a higher contingency of results; high-quality double-blind

trials were lacking, so further exploration is needed. Moreover, the reliability and validity of FMA and ARAT have been validated globally, but their application varies across countries, and they are less applied in the Chinese mainland, so we suggest that FMA and ARAT be used more for analysis in the future^[41]

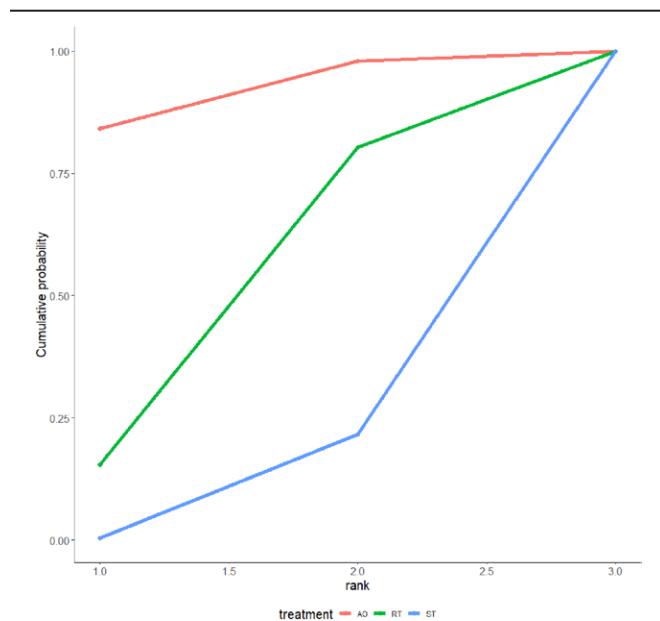


Figure 8. Cumulative probability diagram for MBI. MBI = modified Barthel index.

4.3. AO: Best intervention for improving MBI

ADL of stroke patients is closely linked to UEMF. MBI possesses good reliability and validity as a tool for assessing the ADL of stroke patients.^[42] This study showed that 10 rehabilitation therapies, especially AO, could all improve the ADL of hemiplegic patients with stroke. The core of AO lies in the mirror neuron theory, i.e., when a person observes and imitates another's movements, neurons that encode the action in the motor system of the observer's cerebral cortex will be activated, and mirror neurons have interactions so that patients can master new motor skills.^[43,44] When hemiplegic patients with stroke observe the movements in training, their mirror neurons controlling the same movements can be activated and become more excited, allowing them to be more capable of completing the training. Following 4 weeks of OA for 8 hemiplegic patients with stroke, Errante et al^[45] found that the ADL became significantly better than before. Hsieh et al^[46] investigated the changes in relative alpha and beta powers following AO and motor imagery training and found that AO can induce stronger cognitive activities. This study reached similar conclusions to all of the above studies. However, AO was implemented in only 2 included studies, leading to a higher contingency of results; high-quality double-blind trials were also lacking, so further exploration is needed.

4.4. Limitations

Some limitations are worth noting. First, only English-language databases were searched, so only a few studies were included, possibly leading to publication bias due to an insufficient sample size. Second, the overall quality of the included studies was low, possibly affecting the reliability of the results. In addition, it

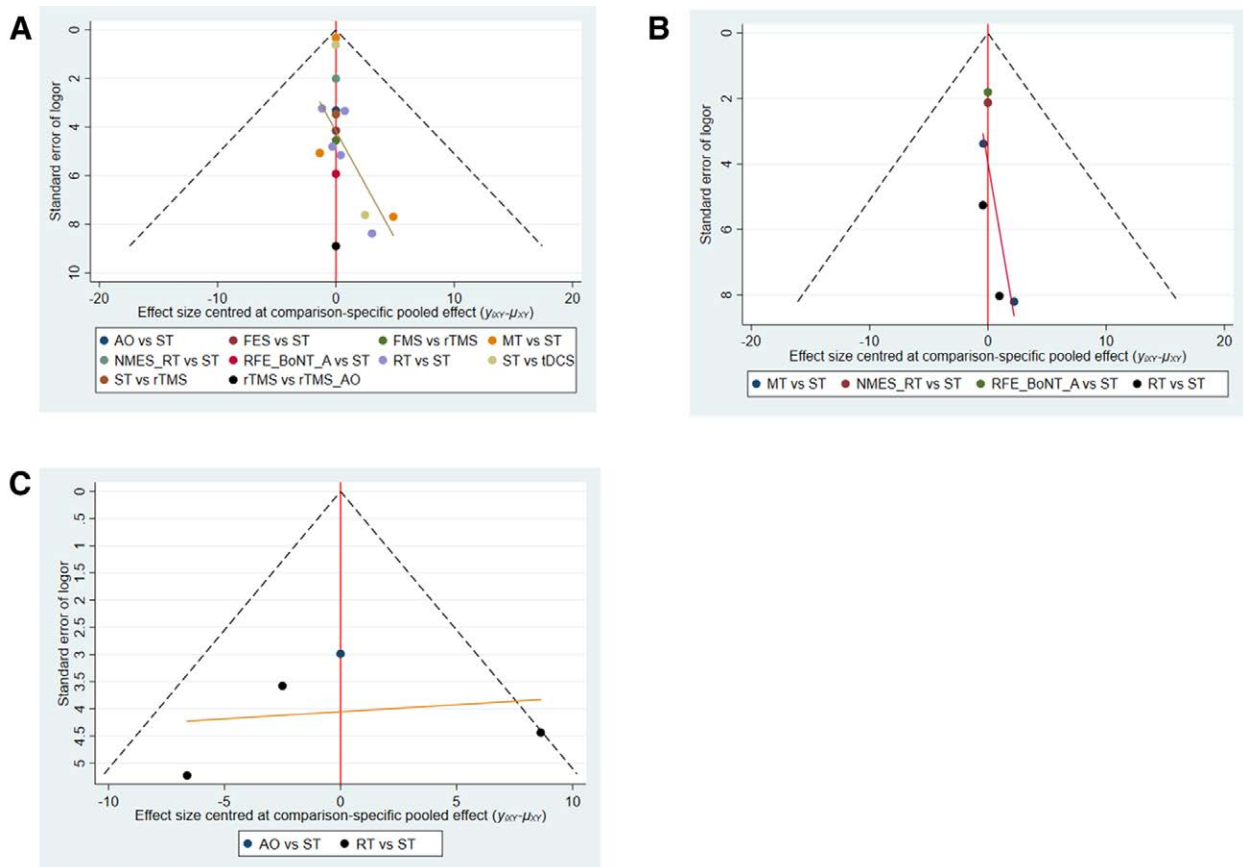


Figure 9. Comparison-adjusted funnel plots. AO = action observation, FMA = Fugl-Meyer assessment of motor recovery, FMS = functional magnetic stimulation, NMES = neuromuscular electrical stimulation.

was difficult to implement blinding of participants and personnel due to the specificity of interventions, and the deficiencies in allocation concealment and blinding might produce great heterogeneity, thus affecting the reliability of results. Given these limitations, more high-quality clinical trials are required to further validate the findings by direct comparisons, and caution should be exercised when selecting more appropriate rehabilitation therapies according to patient needs.

5. Conclusion

This NMA was conducted on the effects of 10 rehabilitation therapies on UEMF and ADL in hemiplegic patients with stroke, and 17 RCTs were finally included. RFE + BoNT-A was identified as the best intervention for improving UEMF, and both AO and RT were remarkably effective in enhancing ADL in hemiplegic patients with stroke. In clinical practice, medical staff should select the most suitable rehabilitation therapy to improve UEMF and ADL in hemiplegic patients with stroke according to their characteristics and objective conditions. Since some limitations were present, large-sample, multicenter, high-quality RCTs are necessary in the future to provide evidence for the selection of rehabilitation therapies for hemiplegic patients with stroke.

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