Systematic Reviews

RESEARCH Open Access

Repetitive transcranial magnetic stimulation for motor function in stroke: a systematic review and meta-analysis of randomized controlled studies

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Abstract

Objective This study aimed to systematically evaluate the safety and effectiveness of repetitive transcranial magnetic stimulation (rTMS) in treating motor dysfunction in stroke patients.

Methods A systematic search was conducted in five online databases, namely, Medline, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, and SPORTDiscus, from their inception to July 29, 2024. Studies meeting the predetermined inclusion criteria were included. The data were analyzed using RevMan 5.4.1 software and Stata 15.0. The subgroup analysis was conducted based on various disease stages and intervention frequencies. The overall effects were estimated using either the fixed effects model or the random effects model, with standardized mean differences (SMDs). The level of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework.

Results A total of 70 studies encompassing 2951 stroke survivors were included. The results of the quantitative analysis revealed that the application of 1 Hz rTMS over the contralesional primary motor cortex (M1) significantly improved motor function during both the early stage (< 1 month) with moderate effect size ($n = 443$, SMD = 0.44, 95% CI 0.24 to 0.63, $P < 0.00001$, $I^2 = 47\%$, fixed-effect model) and recovery period (1–6 months) with moderate effect size ($n = 233$, SMD = 0.61, 95% CI 0.34 to 0.87, $P < 0.0001$, $I^2 = 33\%$, fixed-effect model). In the context of activities of daily living (ADLs), the application of 1 Hz rTMS over the contralesional M1 can lead to improvements in ADLs among individuals in the early stages of stroke with moderate effect size ($n = 343$, SMD = 0.67, 95% CI 0.44 to 0.89, $I^2 = 79\%$, $P < 0.00001$, fixed-effect model). However, evidence to support that 1 Hz rTMS over contralesional M1 can improve motor dysfunction in the chronic phase of stroke (> 6 months) is insufficient.

Conclusion Moderate- to high-quality evidence suggests that 1 Hz rTMS over the contralesional M1 may enhance motor function and independence in ADL during the early stages of stroke and the recovery period (within 6 months) with moderate effect. Nonetheless, as for the efficacy of 3, 5, 10, and 20 Hz rTMS in the treatment of motor

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dysfunction after stroke, it needs to be further determined. It is important to interpret these findings with caution in clinical practice due to the small sample sizes and low quality of the studies reviewed.

Systematic review registration INPLASY, Registration number is INPLASY202360042. DOI number is https://doi.org/10.37766/inplasy2023.6.0042.

Keywords Stroke, Repetitive transcranial magnetic stimulation, Motor function, Systematic review, Meta-analysis

Introduction

Stroke is a prominent contributor to mortality within the realm of noncommunicable diseases, and simultaneously serving as a primary instigator of incapacitation [1]. Approximately 34% of worldwide aggregate health care expenditures are allocated to stroke. Stroke affects individuals across various age groups, with over half of patients experiencing motor dysfunction. This impairment significantly impedes their ability to perform daily activities, consequently placing an increased burden on their families [1]. Approximately 80% of stroke patients experience motor dysfunction in either their upper or lower limbs following a stroke [2, 3]. Approximately 80% of individuals with mild paresis attain full upper limb function, whereas only 20% of those with severe paresis achieve the same level of function [2]. Only 50% of individuals who initially experienced upper limb paralysis exhibited partial motor recovery after a 6-month period [4, 5]. Approximately 70% of individuals with lower limb impairment are unable to walk independently soon following stroke, and only half of these individuals have independent walking function after rehabilitation [4, 5]. Upper and lower limb paresis stands out as a significant predictor of long-term functional recovery following a stroke [4, 5]. Consequently, numerous innovative therapeutic interventions have been suggested with the objective of augmenting motor recuperation [6]. Nevertheless, current medical interventions lack targeted therapies aim to restore function by repairing damaged tissue.

Noninvasive brain stimulation (NIBS) has been explored as a treatment for stroke populations [7–9]. There are several theoretical models that support the use of noninvasive brain stimulation techniques. Among them, the most prominent models are the interhemispheric competition model, the vicariation model, and the bimodal balance-recovery model. According to the interhemispheric competition model, a model of hemispheric interaction, mutual, balanced inhibition exists between the two hemispheres of the brain in healthy individuals [10, 11]. During stroke, damage to one hemisphere disrupts this balance: The affected hemisphere's inhibition of the unaffected hemisphere weakens, and inhibition of the unaffected hemisphere consequently increases [12]. As a result, the affected hemisphere suffers from "double-disabled" and is therefore too inhibited [12]. In healthy individuals, interhemispheric inhibition (IHI) decreases before unilateral index finger movement begins, but reversibly shifts to promote movement [13, 14]. Stroke patients who have recovered relatively well can use the affected hand for movement of the index finger, and the lack of suppression-reversal promotion may interfere with the movement of the affected side, causing this mechanism to fail [13–15]. The vicariation model suggests that the activity of the unaffected hemisphere contributes to functional recovery after stroke, and this recombination pattern is called the compensatory model: That is, the activity of brain areas outside the lesion compensates for the function of the damaged brain area, including the activity of the contralateral undamaged hemisphere [16, 17]. The bimodal balance-recovery model introduces a new concept of structural reserve and defines it as the extent to which neural pathways and relays spared by the lesion contribute to recovery in an individual patient. The main idea of this model is that the degree of structural retention (e.g., retention of motor areas and the corticospinal tract) determines which of the interhemispheric competition models or the compensatory model is dominant. When degree of the structure retention is high, the interhemispheric competition model can better predict the degree of restoration. When the degree of structure retention is low, the compensatory model is dominant [15].

Transcranial magnetic stimulation (TMS), a form of NIBS, involves the application of an insulated coil to the scalp and targets a precise region of the brain. Upon the passage of an electrical current through this coil, the resulting magnetic signal can traverse the scalp and skull without any loss of intensity, thereby influencing brain metabolism and neural activity [7, 8]. This phenomenon induces the trans-synaptic activation of pyramidal cells, resulting in the generation of descending volleys within the pyramidal axons that project onto spinal motoneurons, commonly referred to as the corticospinal tract [18]. Motor neuron activation resulting from corticospinal projections induced by TMS can be measured as motor-evoked potentials (MEPs) using surface electromyography. The activation of motoneurons in response to corticospinal volleys elicited by TMS leads to contraction in a specific muscle, thereby evoking an MEP that is captured by electromyography (EMG) via surface

electrodes placed over the muscle belly. The amplitude of the MEP's peak-to-peak measurement is employed to estimate the excitability of the corticospinal tract [19, 20]. Substantial evidence suggests that the mechanism underlying the aftereffect of rTMS resembles to both long-term potentiation (LTP) and long-term depression (LTD) [19, 21]. Since the introduction of rTMS, a substantial body of research has been dedicated to investigating its impact on motor dysfunction following stroke, as evidenced by the growing number of scholarly publications over time. Currently, low-frequency rTMS (LF-rTMS, typically ≤ 1 Hz) is commonly administered over the unaffected cortex, whereas high-frequency rTMS (HF-rTMS, > 1 Hz) is typically administered over the affected cortex [22].

However, the findings of prior studies investigating the efficacy of rTMS for addressing motor impairment following stroke have yielded inconclusive and conflicting results. The initial Cochrane review did not provide support for the utilization of rTMS in stroke rehabilitation [23]. Conversely, another systematic review and meta-analysis conducted during the same time frame concluded that rTMS has a favorable impact on motor recovery among stroke patients [24]. The ongoing debate surrounding the impact of rTMS on motor function following stroke persists. A recent systematic review, published in 2022, highlighted the potential of rTMS therapy to enhance the outcomes of poststroke sequelae, specifically by ameliorating upper limb function, hand dexterity, and muscle tonicity [25]. However, a subsequent systematic review conducted in the same year demonstrated that NIBS, which includes rTMS, was unable to effectively alter the Fugl-Meyer Assessment Upper Limb (FMA-UL) subscale score among individuals with chronic stroke [26]. Furthermore, significant variability exists in the findings of contemporary research regarding the optimal timing of rTMS intervention. A systematic review has suggested that the efficacy of excitatory rTMS in promoting upper limb motor function recovery is limited to the initial 3 months following a stroke [27]. Interestingly, another study revealed that the effects of real and sham rTMS did not significantly differ within a 3-month period following a stroke [28]. According to a recent systematic review, rTMS significantly improved in upper limb and fine motor function in the short term (0–1 month) and medium term (2–5 months). However, no significant improvement was observed in long-term upper limb function (6 months or more) [25].

In addition, the rapid expansion of publications and ongoing research have exacerbated the challenge of remaining current with empirical contributions and extensive research trajectories. As a result, synthesizing definitive evidence from previous studies is increasingly intricate. Within this framework, reviews play a crucial role in aggregating literature findings, enhancing the knowledge base, identifying theoretical, practical, and methodological gaps, and refining research agendas. However, the issue of ensuring reliability and objectivity in systematic reviews remains a significant challenge that necessitates resolution. To enhance the reliability and transparency of systematic reviews, numerous ongoing studies advocate for the integration of both quantitative and qualitative methodologies. These approaches aim to improve systematic reviews by systematically reorganizing and synthesizing the findings from existing literature [29]. Thus, this study carried out systematic review and meta-analysis to assess the effectiveness and safety of rTMS in addressing motor dysfunction following stroke which is imperative, with the aim of offering valuable insights for the healthcare decisions, patients, and their families.

Methods

Protocol and registration

The protocol for this systematic review was registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY, Registration number is INPLASY202360042. DOI number is https://doi.org/10.37766/inplasy2023.6.0042). The entire study was conducted in strict adherence to the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions.

Retrieval strategy

A systematic search was conducted in five online electronic databases, namely, EMBASE (via embase.com), Medline (via PubMed), the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, CINAHL, and SPORTDiscus (via EBSCO host), from their inception to September 27, 2023, without any language limitations. Following the completion of the data analysis, the literature was updated until July 29, 2024. Additionally, other research reports were identified by examining the reference lists of the articles. The search strategy employed for Medline via PubMed is presented in Table 1. The search strategy employed for additional databases can be found online in the Supplementary Information (SI).

Inclusion and exclusion criteria

The inclusion and exclusion criteria for the studies were defined as follows:

(1) Population

Studies that exclusively examined adult stroke patients, without any limitations on the type, sever-

Table 1 Search strategy of Medline (via PubMed)

NO	Search strategy
#1	"cerebrovascular disorders"[Mesh] or "brain injuries"[Mesh] or "brain injury, chronic"[Mesh]
#2	"stroke$" [Text Word] or "cva" [Text Word] or "poststroke" [Text Word] or "post-stroke"[Text Word]
#3	"cerebrovasc$" [Text Word] or "cerebral vascular" [Text Word]
#4	"cerebral" [Text Word] or "cerebellar" [Text Word] or "brain$" [Text Word] or "vertebrobasilar"[Text Word]
#5	"infarct$" [Text Word] or "isch?emi$" [Text Word] or "thrombo$" [Text Word] or "emboli$" [Text Word] or "apoplexy"[Text Word]
#6	#4 and #5
#7	"cerebral" [Text Word] or "brain" [Text Word] or "subarachnoid"[Text Word]
#8	"haemorrhage" [Text Word] or "hemorrhage" [Text Word] or "haematoma" [Text Word] or "hematoma" [Text Word] or "bleed$"[Text Word]
#9	#7 and #8
#10	"hemiplegia"[Mesh] or "paresis"[Mesh]
#11	"hempar$" [TW]or "hemipleg$" [TW] or "brain injur$" [TW]
#12	"Gait Disorders, Neurologic"[Mesh]
#13	#1 or #2 or #3 or #6 or #9 or #10 or #11 or #12
#14	Transcranial Magnetic Stimulation[Text Word]
#15	Magnetic Field Therapy[Text Word]
#16	Magnetics[Text Word]
#17	Electromagnetic Fields[Text Word] or Electromagnetic Phenomena[Text Word]
#18	(("magnet$" or "electromagnet$" or "electro-magnet$") adj5 ("stimulat$" or "field$" or "coil$"))[Text Word]
#19	(TMS or rTMS)[Text Word]
#20	#14 or #15 or #16 or #17 or #18 or #19
#21	randomized controlled trial [pt]
#22	controlled clinical trial [pt]
#23	randomized [tiab]
#24	placebo [tiab]
#25	clinical trials as topic [mesh: noexp]
#26	randomly [tiab]
#27	trial [ti]
#28	#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
#29	humans [mh]
#30	#28 AND #29
#31	#13 AND #20 AND #30

ity, location, or progression of the disease, were included. Studies that included multiple conditions, such as stroke combined with Parkinson's disease or spinal cord injury, were excluded from consideration.

(2) Intervention

The intervention utilized in this study involved the application of simple rTMS, specifically low-frequency rTMS or high-frequency rTMS. Patterned rTMS techniques, such as theta burst stimulation (θTBS), continuous TBS (cTBS), intermittent TBS (iTBS), paired pulse stimulation (PPS), quadripulse stimulation (QPS), and paired associative stimulation (PAS), were not included. Importantly, the intervention consisted of a single mode of rTMS and did not involve the combination of two or more different rTMS techniques (e.g., LF-rTMS combined with HF-rTMS). Only studies that utilized rTMS, rTMS combined with rehabilitation therapy, or rTMS combined with conventional medication therapy were included in the experimental group. Studies that combined rTMS with electrical stimulation (e.g., transcranial direct current stimulation (tDCS) or transcutaneous electrical nerve stimulation (TENS)) or rTMS with specific drugs (excluding routine medications for stroke) were excluded. The intervention parameters, including time, coil position, frequency, intensity, and duration, were not restricted.

(3) Comparison

Control groups included sham-rTMS, sham plus rehabilitation, rehabilitation, or no treatment. Studies that did not have appropriate control groups or sham intervention groups were excluded from the analysis [30]. Studies that utilized patterned rTMS as an intervention for the sham group were excluded from the analysis [31].

(4) Outcome

The primary outcome of this study was motor function, with no limitations on the instruments used for measurement (e.g., FMA-UL, Fugl-Meyer Assessment for lower limb (FMA-LL), and grip strength). The secondary outcomes included activities of daily living (ADLs), adverse events, and dropout, with no restrictions on the measurement tools employed.

(5) Study

In terms of study design, only randomized controlled trials (RCTs) were included in this study. In the case of cross-over studies, only the initial segment that adhered to the study protocol was considered. The minimum requirement for total participants was set

to 6. The inclusion criteria were restricted to publications in the English language.

Study selection and data extraction

Acquisition, screening, and data extraction were performed between March 2023 and September 2023, and this process was updated to July 29 2024. All acquired documentation was carried out using Endnote X7. Following the removal of duplicate references, two authors (XGL and TW) independently assessed the title and abstract of the literature reports to identify potentially eligible studies. The final selection of included studies was based on reading the full text, in accordance with the preestablished inclusion criteria.

The data extraction process was conducted by a single researcher (DL) using a preestablished table, which was subsequently reviewed by another researcher (ZLM). The extracted data encompassed various components, including but not limited to the following: (1) Fundamental details (such as authors, title, publication date, number of participants, sex, age, duration, stroke location, and severity). (2) Methodological quality indicators (such as the randomization method, allocation concealment, operator blinding, presence of a sham stimulation group, statistician blinding, and intention-to-treat analysis). (3) The interventions included various parameters, such as the placement and shape of the coil, as well as the intensity, frequency, duration, and follow-up period. (4) The outcomes of interest included both primary and secondary outcomes, which were assessed using specific evaluation tools. Additionally, follow-up assessments, drop-out rates, and adverse events were also considered. In cases where raw data were not provided, data extraction software (Getdata 2.2) was used to obtain relevant information from statistical charts, such as line charts or bar charts (SHM and LL). To ensure the precision of data extraction, data were exclusively employed for analysis when the consistency of independently extracted data by two authors surpasses 95%. Any missing data were acquired through communication with the original author via email. If no mean was reported, the median was considered as the mean. If no standard deviation was reported, then the standard deviation was calculated from the confidence interval or interquartile range. Data were managed and transformed using Microsoft Excel. Data were analyzed using RevMan 5.4 and Stata (version 15.0). In instances of incongruity during the literature screening and data extraction process, consensus was reached after consulting with a third author possessing substantial expertise (LJL).

Research quality assessment

The methodological quality of the included studies was assessed by two independent reviewers (ZCY and LL) using the "Risk of Bias 2" table. This table evaluated six domains, namely, selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases. Each domain consisted of one or more entries. Selection bias included random sequence generation and allocation concealment, whereas performance bias involved the blinding of participants, rTMS intervention operators, and rehabilitation therapists. Detection bias encompasses the blinding of outcome assessments and data analysts, whereas attrition bias encompasses incomplete outcome data, reporting bias, and selective reporting. To evaluate the extent of bias, each entry in every study was categorized as low risk, high risk, or unclear. In instances of incongruity during process of risk assessment, consensus was reached after consulting with a third author possessing substantial expertise (LJL).

Data analysis

Overall effects

The Cochrane Review Manager (RevMan 5.4) and Stata 15.0 software programs were used for data analysis. To evaluate the overall effects, standardized mean differences (SMDs) or mean differences (MDs) with 95% confidence intervals (95% CIs) were employed for continuous data. According to Cochrane guidelines and literature [32, 33], the SMD should be used to evaluate overall effects in specific scenarios to mitigate the impact of inter-study variability on results. These scenarios include as follows: firstly, when different measurement units are used to assess the same outcome; secondly, when diverse measurement tools and methodologies are applied to the same outcome; and thirdly, when there is significant variability or a doubling in outcome values across different studies. In situations not characterized by these conditions, the MD is recommended for data synthesis. In this study, although a consistent measurement tool was used for assessing the primary outcome of motor function (encompassing both upper and lower limbs), the reported values across studies demonstrated considerable variability. Consequently, the SMD was employed as the index for data synthesis. Furthermore, for outcome measures such as motor function assessed via the Modified Ashworth Scale (MAS) or Ashworth Scale (AS), activities of daily living (ADLs) (via Modified Barthel Index(MBI) or Barthel Index (BI)), and neurological function (via National Institute of Health stroke scale (NHISS), resting motor threshold (RMT), or motor evoked potentials(MEPs)), the use of differing

measurement units or tools necessitated the selection of SMD for these outcomes as well. According to the Cochrane criteria, an absolute SMD value of approximately 0.2 is indicative of a small effect, around 0.5 represents a moderate effect, and a value of 0.8 or higher indicates a large effect size. The pooled effect was estimated using either the fixed-effect model or random-effect model, depending on the results of chi-square test and Higgins I^2 value. Statistical heterogeneity was assessed using the chi-square test and Higgins I^2 value. A significant level of statistical heterogeneity was observed: if a chi-square test results $P<0.1$ and $I^2>75\%$, in which case a random effects model is used; otherwise, a fixed effects model is used.

Subgroup analysis

Subgroup analysis was conducted to identify clinical heterogeneity based on the varying frequencies of rTMS (1 Hz, 3 Hz, 5 Hz, 10 Hz, 20 Hz) and different disease periods (< 1 month, 1–6 months, > 6 months). The duration of early rehabilitation was defined as less than 1 month from stroke onset, the recovery period was considered to be between 1 and 6 months, and chronic rehabilitation was defined as more than 6 months, following the guidelines [34]. In studies encompassing patients with stroke episodes spanning multiple time periods as defined by our study, we calculated the mean stroke time or percentage of the population in each period to ascertain the specific time period under consideration.

Sensitivity analysis

The robustness of results was assessed using sensitivity analysis. In this study, a comprehensive sensitivity analysis was conducted at each decision node, encompassing literature search, literature inclusion, data extraction, and data analysis, to evaluate the impact of these decisions on the study results. Detailed analytical procedures and corresponding processing methods are documented in Supplementary Information (SI) Table S1. At the statistical method selection stage, either a random effects model or fixed effects model was applied to evaluate the overall effect. Furthermore, Stata software (Version 15.0) was utilized to sequentially exclude studies one by one and subsequently re-perform the meta-analysis to evaluate the robustness of the results. A significant alteration in the pooled effect size following the exclusion of a specific study suggested its considerable impact on the overall findings.

Publication bias

In cases where the reported outcomes consisted of more than five studies or involved a participant pool exceeding 250 individuals, Egger's test was conducted to investigate the presence of publication bias.

Grading the quality of evidence

The evidence level was evaluated via the GRADEprofile software version 3.6, in accordance with the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework. The assessment considered five factors for downgrading the evidence (risk of bias, inconsistency, indirectness, imprecision, publication bias) and three factors for upgrading the evidence (large effect, plausible confounding that could alter the effect, dose–response gradient). Based on this evaluation, the evidence quality was categorized as high, moderate, low, or very low.

Results

Study identification

A comprehensive search of online databases yielded a total of 7006 articles. Among these, 3069 records were identified as duplicate reports, while 3937 records were deemed irrelevant based on abstracts and titles by two reviewers. Subsequently, 176 full texts were carefully screened, resulting in the exclusion of 111 records that did not meet the inclusion criteria. Additionally, five records were included in this study through reference screening. A total of 70 RCTs meeting the predetermined inclusion criteria were ultimately included in this systematic review. Not all studies included in this research reported the necessary outcome indicators for quantitative analysis, specifically FMA-UL, FMA-LL, MAS/AS, MBI/BI, NIHSS, and RMT. To address this gap, the original authors of these studies were contacted via email to inquire about the availability of the relevant data. By the time of revision, responses were received from nine authors, all of whom indicated that they had not collected the specified outcome indicators. Ten authors did not respond. As a result, the 19 studies lacking these indicators were included exclusively in the qualitative analysis, while the remaining 51 papers were incorporated into both qualitative and quantitative analyses. The complete procedure of the literature screening is depicted in Fig. 1.

Study characteristics

(1) Population

The pertinent details of the studies included in this analysis are presented in Table 2 and Table 3. The aggregate number of participants encompassed 2951 individuals, with participant counts varying between 9 and 240. Within the experimental group, the number of participants ranged from 4 to 132, whereas the control group included participants ranging from 5 to 160. The female proportion ranged from 13.33 to 78.38%, and the mean

age of participants ranged from 49.7 to 79 years. The study included patients with illness durations ranging from 6 h to more than 12 months, with 5 studies failing to report the type of stroke [35–39], 30 studies including only ischemic stroke patients [28, 40–68], and 35 studies including both ischemic and hemorrhagic stroke patients [39, 69–102]. Among the included studies, 19 studies did not provide information on the severity of the patients [36, 37, 39–41, 43, 45, 49, 54–57, 60, 61, 63, 65, 68, 86, 90], while the remaining studies reported the severity of the included patients. Of these, seventeen studies included patients with mild to moderate or to severe impairment [28, 38, 42, 45–48, 58, 59, 69, 77, 81–83, 95, 98, 99], and various assessment methods, such as independent walking of 10 m [80, 102], or walk 10 m with assistance [80], minimum 10° of volitional flexion and extension of fingers and wrist in the affected limb [67], the Brunnstrom scale [28, 51, 62, 71, 77, 97, 99–101], Fugl-Meyer Assessment (FMA) [58, 74, 91, 99, 103], functional ambulation classification (FAC) [72, 79, 96], National Institute of Health stroke scale (NHISS) [46, 64, 92, 98], Modified Rankin Scale (MRS) [35], Timed Up and Go Test (TUGT) [78], Movement-related cortical potential (MRCP) [58], the Medical Research Council (MRC) Scale [59], Glasgow Coma Scale (GCS) [87], Chedoke–McMaster [44], Modified Ashworth Scale (MAS) [62, 70, 71, 88], Lovett scale [52], and Bruininks–Oseretsky Test (BOT) [94], were employed to determine the functional status of the included patients in other studies.

(2) Intervention

In the experimental group, eight studies used transcranial magnetic stimulation alone [41, 44, 48, 58, 72, 80, 85, 88]. Other studies integrated a combination of rTMS with diverse rehabilitation training approaches, including physical therapy (PT), occupational therapy (OT),

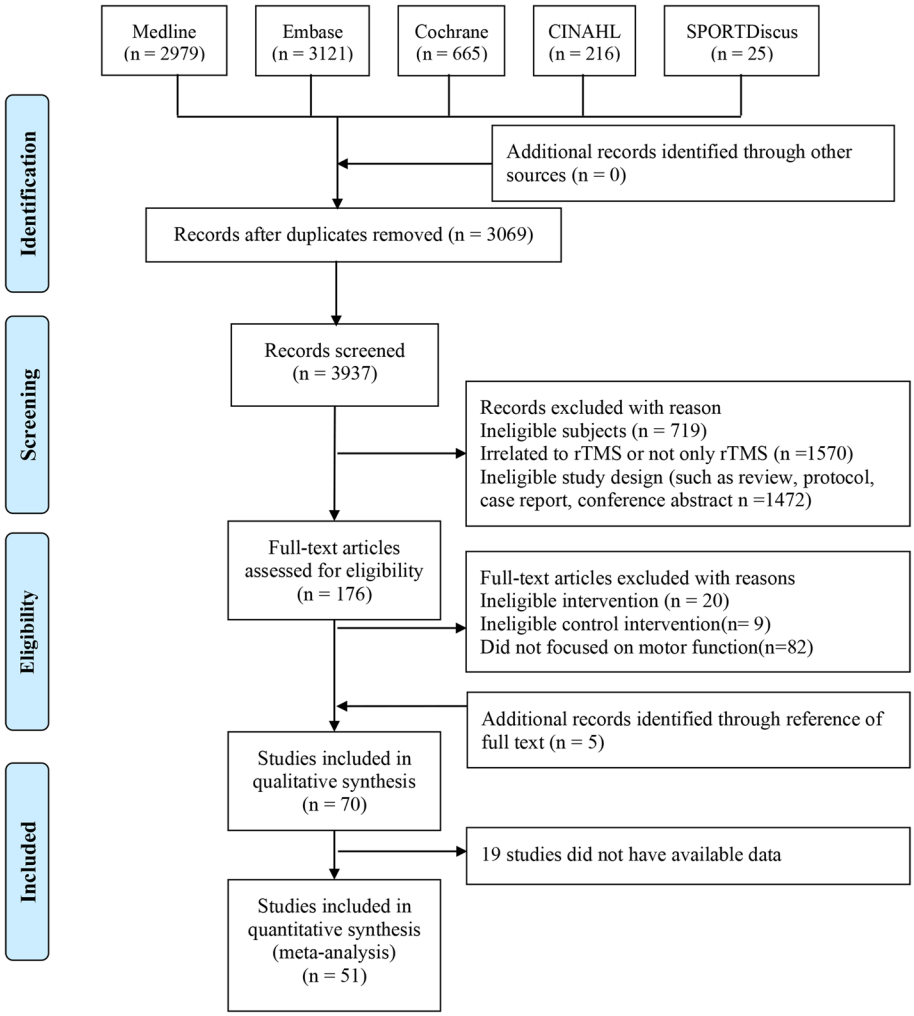

Fig. 1 Flow diagram of the study selection process

Table 2 Characteristics of included studies in this systematic review

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Abdelkader 2024 [92]	30/10	9/36	54.9/51.8	Duration of 2 weeks to 6 months	IS and HS	Minor (1–4) to moderate (5–15) National Institutes of Health Stroke Scale (NIHSS)	rTMS + Conventional rehabilitation	1000 pulses, 90% RMT. Excitatory group: 5 Hz, 10 s duration alternating with five sham trains of inhibitory 1 Hz rTMS of 10 s Inhibitory group, five trains of inhibitory 1 Hz rTMS, each of 10 s, alternating with one excitatory sham 5 Hz train of 10 s	70 mm figure-8 coil/Excitatory group: ipsilesional M1 Inhibitory group: contralesional M1	Sham rTMS rehabilitation	Sham stimulation was applied over the optimal site by position	FMA, WMFT
Aşkın 2017 [40]	20/20	11/29	58.8/56.8	>6 months /chronic	IS	DR	rTMS + PT	1200 pulses, 1 Hz, 90% RMT, 20 min, 10 sessions, 5 days/week, 4 weeks	Figure 8 coil /contralesional M1	PT: 5 days/week, 4 weeks, 20 sessions	NA	BRS, FMA-UL, BBT, MAS, FIM, MMSE, FAS
Avenanti 2012 [69]	16/14	14/16	62.3/64.0	>6 months /chronic	IS and HS	Mild upper limb motor deficit	rTMS + PT	1500 pulses, 1 Hz, 90% RMT, 25 min, 10 days, 2 time-locked daily interventions	70-mm focal coil /contralesional M1	Sham rTMS PT: 45 min of standard task-oriented upper-limb exercises	Same parameters with no current	JHFT, BBT, NHPT, Maximal force of key grip, tip-pinch, dynamometer
Barros 2014 [70]	10/10	7/13	57.4/64.6	≥6 months /chronic	IS and HS	Muscle tone at the wrist with a MAS score between 1 and 3	rTMS + PT	1500 pulses, 1 Hz, 90% RMT, daily, 10 sessions	70-mm Fig. 8 coil /contralesional M1	Sham rTMS PT: 30 min, 3 days/week, 10 sessions	A coil disconnected from the stimulator unit was held over the scalp while a second coil, connected with the stimulator, was positioned behind the patient's head, without touching the scalp	Wrist MAS, FMA-UL, FIM, Wrist ROM, SSQOL, SSQOL-UE
Blesneag 2015 [41]	8/8	6/10	69/69	10 days /acute	IS	DR	rTMS	1200 pulses,1 Hz, 120% of RMT, once per day, 20 min, 5 days/week, 10 sessions	Figure 8 coil /contralesional M1	Sham rTMS	The coil at the same location but with an intensity of 10% of RMT, which provided a skin sensation similar to real stimulation	FMA-UL, RMT, RP, AM parameter

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Chen 2023 [71]	30/30	21/39	58.8/58.1	1–6 months /subacute	IS and HS	The Brunnstrom stage of the damaged lower limb between II and V; according to the improved Ashworth spasm assessment, the lower limb muscle of the patient was in spasm with spasmodic foot ptosis varus gait (limited ankle dorsiflexion, with varus) and the grade reached level 2 or greater	rTMS + MRP + Routine rehabilitation	1200 pulses, 1 Hz, 90% RMT, 20 min once a day, 6 days a week for 4 weeks	Circular coil /contralesional M1	MRP + Routine rehabilitation MRP: 20–30 min every day for 4 weeks Routine rehabilitation:40 min of training once a day, 6 days a week, 4 weeks	NA	MAS, FMA-UL, FMA-BL, Brunnstrom score, Hoffer walking score
Chervyakov 2018 [35]	24/10	14/20	56.6/61.4	Between 1 and 12 months (mean stroke onset is 6.45 ± 5.91 month) /chronic	DR	Stroke severity of four points or less as determined by the MRS	rTMS + PT	**LF group:** 1200 pulses, 1 Hz, 100% RMT, 2 min, 5 days/week, 10 sessions, 2 weeks **HF group:** 200 pulses, 10 Hz, 80% of RMT, 10 min, 5 days/week, 10 sessions, 2 weeks	70-mm Fig. 8 coil /LF: contralesional M1 HF: ipsilesional M1	Sham rTMS, PT: 45 to 55 min, 5 days/week, 10 sessions, 2 weeks	The coil was placed over the confirmed cortical representation of the APB muscle but was not connected to the stimulator. The sham procedure imitated the HF stimulation protocol, and the patient could hear all the real sounds but without actual exposure to the electromagnetic field	FMA, MAS, BI
Chieffo 2021 [80]	6/6	6/6	58.7/61.2	>6 months /chronic	IS and HS	Able to walk with/without stick for at least 10 m but in more than 10 s, ability to walk independently	rTMS	1600 pulses, 90% RMT, 20 Hz, 40 2-s trains, 20 s intertrain interval, 15 min, five in the first week and three in the second and third weeks	H Coil I /leg motor cortex	Sham rTMS	Activating a sham circuit placed in the same stimulation helmet, designed to mimic a similar acoustic artifact and some scalp sensation but without inducing an effective field inside the brain	FMA-LL, MAS,10MT,6MWT

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Conforto 2012 [42]	15/15	12/18	54.8/56.7	5–45 days (mean stroke onset is 27.5 day) /acute	IS	Mild to severe hand paresis	rTMS + outpatient customary rehabilitation	1500 pulses, 90% RMT, 1 Hz, 25 min, 5 days/week, 10 sessions, 2 weeks	Figure 8 coil /contralesional M1	Sham rTMS outpatient customary rehabilitation: 60-min rehabilitation treatment	In the sham group, the coil was held perpendicularly to the vertex	Jebsen–Taylor test (JTT), force of the lateral pinch of paretic hand, Ashworth, FMA, MRS
Du 2016 [36]	46/23	24/45	56.8/53.7	3 to 30 days /acute	DR	DR	rTMS + PT + medical therapies	**HF group:** 1200 pulses, 80–90% RMT, 3 Hz, 10 s, ITI 10 s, 40 trains, daily, 5 days **LF group**: 1200 pulses, 110–120% RMT, 1 Hz, 30 s, ITI 2 s, 40 trains, daily, 5 days	Figure 8 coil /HF group: affected hemisphere M1 LF group: unaffected hemisphere	Sham rTMS PT: 1 h, daily medical therapies	Same parameters (noise, time and frequency) as the 1-Hz rTMS group over the unaffected hemisphere but with the coil rotated 90° away from the scalp so that no current was induced in the brain	FMA, MRC, NIHSS, BI, MRS
Du 2019 [43]	40/20	12/48	55/56	< 14 days /acute	IS	DR	rTMS + PT + medical therapies	**HF group:** 1200 pulses,100% RMT, 10 Hz, 4 s per session, 40 s interval, 30 sessions per treatment, daily for 5 days **LF group:**1200 pulses, 100% RMT, 1 Hz, 120 s per session, 40-s interval, 10 sessions per treatment, daily for 5 days	Figure 8 coil /HF: ipsilesional M1 LF: contralesional M1	Sham rTMS PT: 1 h, daily	Same parameters (noise, time and frequency) as the LF-rTMS group on M1 of the unaffected hemisphere but with the coil rotated 90°away from the scalp, so that minimal or no current flow was induced in the brain	FMA, MRC, NIHSS, fMRI ROI
Edwards 2023 [47]	31/29	18/42	59/58	3 to 12 months, 55% more than 6 months/ chronic	IS	Chedoke–McMaster arm and hand stage of 3–6	rTMS	1 Hz, 900 pulses, 110% RMT, 60 min, 3/week, 6 weeks	DR the shape of coil /contralateral M1	Sham rTMS, motor therapy: 60-min structured session of goal-directed, task-oriented rehabilitation therapy, 6 weeks	The sham stimulation was delivered in a single 1-Hz pulse train of 900 pulses given using a Sham coil	FMA-UL, Action-Research Arm Test, NHISS, EQ-5D
El-Tamawy 2019 [45]	20/20	12/28	57/57	< 6 months /subacute	IS	DR	rTMS + PT	1 Hz, 90% of AMT, 20 min, daily, two weeks, 10 sessions	70-mm Fig. 8 coil/ contralesional M1	PT: daily, 2 weeks	NA	FMA-UL, hand grip dynamometer for grip strength
El-Tamawy 2020 [46]	20/20	12/28	57.2/57.5	< 6 months /subacute	IS	Mild to moderate motor impairments according to the NIHSS	rTMS + PT	1200 pulses, 90% RMT, 1 Hz, 20 min, 10 trains, 10 s and 5 s wait time, daily, 5 days/week, two consecutive weeks	70-mm Fig. 8 coil /contralesional M1	Sham rTMS PT: daily, 2 weeks	Sham rTMS session was applied by titling the coil 45°over the M1 area	MAS, cRMT, iRMT

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Emara 2010 [47]	40/20	20/40	52.9/55.9	>1 month (mean stroke onset is 3.1 months) / subacute	IS	Mild to moderate hand weakness	rTMS + PT	Group I: 7500 pulses, 5 Hz, 2.5-min pulse, 80–90% RMT, daily, 10 days Group II: 1500 pulses, 1 Hz, 2.5-min pulse, 110–120% RMT, daily, 10 days	Figure 8 (MC-B70) coil /Group I: ipsilesional M1 Group II: contralesional M1	Sham rTMS PT: daily, 2 weeks	Same parameters as for group II over the contralesional hemisphere but with the coil angled at 90° from the scalp using the same stimulation parameters	FT-r, AI scores, MRS
Fang 2024 [96]	18/18	10/26	58.7/57.0	1 to 6 months after stroke onset /subacute	IS and HS	Brunnstrom Recovery Stage of the lower limb of 3–5; capable of independent walking for more than 15 m (with or with-out supervision); FAC level less than 4	rTMS + Augmented reality gait adaptive training	1 Hz, 20 min and consisted of a series of 2-s trains, delivering a total of 600 pulses with 8-s intertrain intervals, five consecutive daily sessions, 20 sessions, 4 weeks	Contralesional M1	Augmented reality gait adaptive training a total of 20 sessions, conducted over 4 weeks with five consecutive daily sessions	NA	FMA-LL, Surface electromyography data, BBS,
Forogh 2017 [72]	26	10/16	53/79	>1 month /84.6% was more than 6 months /chronic	IS and HS	Ability to perform 3-step command; impaired patient's balance and gait, the ability to walk with or without support, and with FAC more than one	rTMS	1200 pulses, 1 Hz, 90% MT, 20 min, 5 days	70-mm Fig. 8 coil /contralesional M1	Sham rTMS	A small speaker was installed on the stimulation coil handle. The coil was placed on the head, adjustments were done on the rTMS monitor, but speaker was activated by a switch behind the patient. A sound mimicking the real rTMS was played for the patient	Static postural stability, MRC, BBS, FMA
Fregni 2006 [48]	10/5	4/11	57.7/52.6	More than 1 year /chronic	IS	Mild to moderate motor deficit	rTMS	1200 stimuli, 1 Hz, 100% RMT, 20 min, five sessions	Figure 8 coil /unaffected hemisphere M1	Sham rTMS	For the sham stimulation, we placed the coil at the same place that was used for the motor cortex stimulation and used the same stimulation parameters; however, a sham coil was used	cRT, simple reaction time (sRT), PPT, JHFT
Gong 2021 [37]	15/15	4/26	59.7/63.4	Within 30 days /acute	DR	DR	rTMS + PT	1200 pulses, 1 Hz, each sequence was 30 s, 2-s interval, 40 sequences/time, 5 days/week, 4 weeks	MagproR30 magnetic stimulation instrument /contralesional M1	PT: 40 min, once a day, 5 days a week, 4 weeks	NA	NIHSS, FMA-UL, FMA-LL, BI

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Gottlieb 2021 [73]	14/14	16/12	63.9/62.4	At least 2 weeks delay between stroke onset (mean stroke onset is 43 days) /subacute	IS and HS	Functional restriction of an upper extremity	rTMS + rehabilitation therapy	1200 pulses, 1 Hz, 100% RMT, 5 sessions per week, 10 sessions	80-mm Fig. 8 coil /contralesional M1	Sham rTMS regular neurological rehabilitation: 30-min occupational therapy and 10-min passive electrical stimulation with focus on the affected upper limb	The stimulation protocol was equal in both groups, but the sham coil elicited the pulses in the opposite direction, i.e., away from the head	MAS, FMA-UL
Guan 2017 [49]	21/21	12/30	59.7/57.4	Within 1 week /acute	IS	DR	rTMS + rehabilitation therapy	50 trains of 20 pulses, 2 s intertrain intervals, 5 Hz 120% RMT, daily,10 days	Figure 8 coil /ipsilesional M1	Sham rTMS standardized therapies Antiplatelet drugs and motor rehabilitative training	In the sham group, coils were placed perpendicular to the scalp. The patient wore a 10- 20 system EEG cap for scalp location and earplugs to protect their hearing	NIHSS, BI, FMA-UL, FMA-LL,MRS, RMT
Haghighi 2021 [74]	10/10	9/11	50.5/53.9	Less than 6 months (mean stroke onset is 3.1 months) /subacute	IS and HS	FMA-UL score of 22–44	rTMS + rehabilitation therapy	2000 pulses, 20 Hz, 90% RMT, 5 s duration, 50 s intertrain interval, 20 train, three times per week, 10 sessions	100 mm figure-of-eight coil/ ipsilesional M1	RP consisted of a range of motion training, motor control education, the stretch of hypertonic muscles, the practice of activities of daily living, and functional electrical stimulation (for 20 min, with 25 Hz frequency and 0–250 μs pulse wide to obtain controlled muscle contraction)	NA	BBT, FMA-UL, grip strength, pinch strength

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Harvey 2018 [75]	132/67	69/130	59.2/57.6	Within 3 to 12 months (71.4% more than 6 months) /chronic	IS and HS	With a Chedoke assessment stage of 3 to 6 for both arm and hand	rTMS + rehabilitation therapy	900 pulses, 1 Hz, 110% MT, > 15 min, 3 times per week, 18 treatment sessions, 6 weeks	72-mm figure of eight coil /noninjured motor cortex	Sham rTMS, 20-min upper limb therapy and 60-min session of goal-directed, task-oriented rehabilitation therapy	The sham group received 900 sham TMS pulses per session. The sham condition was delivered using a sham TMS coil with identical external physical characteristics as the active TMS coil. Internally, the sham coil was based on a typical figure-of-eight design but with wiring wound in a way that both wings of the figure eight turn in the same direction	FMA-UL, WMFT, ARAT, SIS, EQ-5D, NIHSS, PHQ-9
Higgins 2013 [76]	4/5	3/6	74/60	At least 3 months (mean stroke onset is 112 months) /chronic	IS and HS	Weakness of one arm	rTMS + functional enhancement program	1200 pulses, 1 Hz, 110% RMT, 200 stimulator with 5–10-s interpulse interval, twice weekly, 8 sessions, 4 weeks,	Air-cooled figure-8 coil/ motor cortex of the unaffected hemisphere	Sham rTMS Functional enhancement program: 4 weeks, twice weekly	The sham group received sham-rTMS using a coil that mimics the look and sound of the real coil, ensuring blinding of participants as to group assignment. Sham rTMS procedures were identical to those used for real-rTMS except that a placebo coil was used	BBT, grip strength, pinch strength, SIS, WMFT
Hosomi 2016 [77]	18/21	16/23	62.4/63.2	Within 8 weeks (mean stroke onset is 45.6 days) /subacute	IS and HS	Severity of symptoms (Brunnstrom stages hand score ≤ 3[severe] and ≥ 4 [mild]	rTMS + PT + OT	500 pulses per session, 90% RMT, 5 Hz, 10 trains, 10 s with 50-s intertrain interval, daily, 10 consecutive days except for weekends	Figure 8 coil /ipsilesional M1	Sham rTMS 20 min, 8 sessions, daily rehabilitation, occupational therapy made up 3 sessions per day	Sham stimulations were applied with the same parameters as real stimulations, but the coil was placed at a 90°angle to the scalp	Brunnstrom stages, FMA, Handgrip strength score, NIHSS, FIM, Finger tapping measurement
Huang 2018 [78]	18/20	15/23	62.2/61.2	10–90 days (mean stroke onset 28.5 days) /acute	IS and HS	Displaying substantial leg disabilities and inability to complete a TUGT within 2 min independently even with orthosis Severely disabled patients	rTMS + PT	900 pulses, 1 Hz, 120% AMT, 15 min, daily, 15 sessions, 15 days	A 110-mm double-cone coil/ contralateral M1	Sham rTMS PT: 45 min, daily, 15 sessions, 15 days	Sham rTMS using a customized sham coil	NIHSS, MRS, MMT, TUGT, PASS, POMA-b, BI, FMA-LL, MEP, Balance function, ADL, SSQOL

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Jia 2024 [97]	18/19	15/22	55.6/61.89	Within 6 months after onset (Median stroke day is 21 days and 17 days)/ acute	IS and HS	Function of the affected upper limb below Brunnstrom scale stage IV	rTMS + PT + OT + Graded Motor Imagery	1 Hz, 80% RMT, 20 min, once a day, 5 days a week, for 4 weeks	Figure 8 coil /unaffected M1	PT + OT + Graded Motor Imagery 120 min	NA	FMA-UE, ARAT, MBI, MAL-AOU, MAL-QOM, MEP
Juan 2022 [50]	32/14	8/38	53.6/52	Within 2 weeks/the first month within symptom onset /acute	IS	Unilateral upper limb motor deficit	rTMS + PT	HF group: 1200 pulses, 10 Hz, 100% RMT, 4 s per session, 40 s interval, daily, 5 consecutive days, 30 sessions per treatment LF group: 1200 pulses, 1 Hz, 100% RMT, 120 s per session, 40 s interval, daily, 5 consecutive days, 10 sessions per treatment	Figure 8 coil (outer diameter of 1 wing, 9 cm) /HF group: ipsilesional M1 LF group: contralesional M1	Sham rTMS PT: 1 h, daily, 5 consecutive days Medical therapy	The sham group received rTMS with the same parameters (noise, time, and frequency) as the 1 Hz rTMS group on M1 of the unaffected hemisphere but with the coil rotated 90° away from the scalp so that no current was induced	FMA, MRC, NIHSS, fMRI ROI
Ke 2020 [53]	27/13	20/20	55.7/58.3	Less than 2 weeks earlier /acute	IS	Patients had at least 10 of voluntary flexion and extension of the fingers and wrist in the affected limb	rTMS + conventional physical and medical treatment	Short ITI group: 1200 pulses, 20 Hz, 110% RMT, 2 s stimulation, 8 s interval, 5 min per session, 5 times per week, 10 sessions over 2 weeks Long ITI group: 1200 pulses, 20 Hz, 110% RMT, 2 s stimulation, 28 s interval, 15 min per session, 5 times per week, 10 sessions over 2 weeks	7 cm "8"-type coil /ipsilesional M1	Sham rTMS 30 min of PT and 30 min of OT, 5 times per week, 10 sessions over 2 weeks Conventional drug treatment	For the sham group, the magnetic coil was applied to the hotspot of the APB cortical representative area in the affected side of the brain, but no magnetic stimulation was delivered	BRS, FMA-UL, BI
Khedr 2005 [55]	26/26	16/36	53.8/52.2	Mean stroke onset is 7.2 days /acute	IS	DR	rTMS + conventional physical and medical treatment	3 Hz, 120% RMT, ten 10-s trains with 50 s between each train, daily, 10 days	Figure 8 coil (9-cm outer wing diameter /ipsilesional M1	Sham rTMS Physical and medical therapies	Sham rTMS with the same parameters was applied with the coil angled away from the head to reproduce the noise of the stimulation as well as some local sensation	SSS, NIHSS, BI, RMT, MEPs

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Khedr 2009 [54]	24/12	17/19	56.8/60	7 to 20 days /acute	IS	DR	rTMS + conventional physical and medical treatment	Group 1: 900 pulses, 1 Hz, 15 min, 100% RMT daily, 5 days Group 2: 900 pulses, 3 Hz, 10 s, intertrain interval 2 s, 30 trains, 130% RMT, daily, 5 days	90 mm Fig. 8 coil /Group 1: contralesional M1 Group 2: ipsilesional M1	Sham rTMS Conventional therapy and medical treatment. Daily, 5 days	Sham rTMS with the same parameters of the second group but rTMS was applied with the coil angled away from the head to reproduce the noise of the stimulation as well as some local sensation	Strength of hand grip, Pegboard Tasks, NIHSS, BI, AMT, MEPs
Khedr 2010 [56]	32/16	24/24	58.3/58	5–15 days /acute	IS	DR	rTMS + conventional physical and medical treatment	Group 1:750 pulses, 130% RMT, 3 Hz, 5 s, 50 trains, every day for five consecutive days Group 2:750 pulses at 100% RMT, 10 Hz, 2 s, 37 trains, every day for five consecutive days	90-mm figure of eight coil/contralesional M1	Sham rTMS Same conventional therapy and medical treatment	Patients received sham rTMS with the same parameters of the first group but the sessions were applied with the coil angled away from the head to reproduce the noise of the stimulation as well as some local sensation	Hand grip, Shoulder abduction, Ankle dorsiflexion, Hip flexion, NIHSS, MRS, RMT,AMT, MEP
Kim 2014 [57]	22/10	15/17	67.4/64.8	<3 months (mean stroke onset is 16 days) /acute	IS	DR	rTMS + conventional physical	900 stimuli, 1 Hz, 100% RMT, 15 min, 5 sessions, 5 consecutive days	75-mm-diameter Fig. 8 coil /2 cm below the inion and 2 cm lateral to the midline on the cerebellar hemisphere ipsilateral to the ataxic side, with the handle pointing superiorly, targeting the posterior cerebellar lobe	Sham rTMS Conventional rehabilitation service	For the sham rTMS, the coil was placed perpendicular to the scalp with the same parameters of stimulation to minimize current flow into the skull	10MWT, BBS
Kim 2020 [28]	36/37	28/45	61.2/62.9	Within 90 days (mean stroke onset is 12 days)/acute	IS	Mild to moderate upper limb motor impairment (Brunnstrom hand stage rating of 3 to 5)	rTMS + OT	1800 stimuli, 1 Hz, 100% RMT, 30 min, daily, 2 weeks	88-mm-diameter Fig. 8 coil /contralesional M1	Sham rTMS Occupational therapy, 30 min, daily, 10 days	For the sham rTMS, the coil was positioned perpendicular to the scalp on contralesional M1 with the same intensity and frequency as that in the real rTMS	BBT, FMA, ARAT, Finger Tapping Test, hand grip, pinch grip, lateral prehension, three jaw chuck strength, MAS, K-MBI

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Lin 2015 [79]	16/16	11/21	58.3/62.3	10–90 days (mean stroke onset is 37 days) /subacute	IS and HS	Exhibiting substantial leg impairment; indicated by a FAC score of 0 to 1	rTMS + PT	900 pulses, 1 Hz, 130% MT, 15 min, 15 consecutive weekdays	70-mm figure-8 coil /contralesional M1	Sham rTMS PT: 45 min, daily, 15 consecutive weekdays	The sham rTMS was delivered using a customized sham coil that produced similar sounds to those produced by a real coil	MMT, Brunnstrom stage, MRS, PASS, POMA-b, BI, FMA-LL
Liang 2023 [39]	15/15	9/21	54.1/54.3	Enrolled < 3 months after the stroke event	IS and HS	DR	rTMS + PT	70% of the rMT, 5 Hz	Double-ended circular coil/ ipsilesional M1	Standard physiotherapy	The coil held vertically to the scalp for 20 min to reproduce the noise of the 5 Hz stimulation	FMA-UE, rMT, Latency (ms),MEP (mV)
Long 2018 [81]	21/20	10/31	57/56.9	Within the last 6 months (mean stroke onset is 19 days) /acute	IS and HS	Moderate motor and sensory deficit of the upper limb	rTMS + conventional physical (PT + OT)	1000 pulses, 1 Hz, 90% RMT, daily, 15 consecutive days	-mm circular coil/ contralesional M1	Sham rTMS Conventional physical The PT program was applied for approximately 30 min once daily, 6 days per week. The OT program was applied for 60 min once daily, 6 days per week	The sham group received sham stimulation at the same sites in the same order as the LF-HF rTMS group. The coil was held at an angle of 90° to the scalp to reproduce the noise of 1 Hz or 10 Hz stimulus for 1000 pulses. Sham stimulation over the upsilesional M1 cortex was performed with the coil held at an angle of 90° to the ipsilesional scalp to reproduce the noise associated with the 10-Hz stimulus	FMA, WMFT
Ludemann-Podubecka 2015 [82]	20/20	15/25	65.7/68.3	Within the last 6 months (77.5% more than 1 month) /subacute	IS and HS	Mild to moderate motor and/ or sensory deficit of one hand	rTMS + task-oriented upper-limb motor-training and motor train	900 pulses, 1 Hz, 100% RMT, 15 min, daily, 15 working days	70-mm Fig. 8 coil /contralesional M1	Task-oriented upper-limb motor-training and motor training, 30 min, daily, 15 working days	For sham rTMS a single train of 900 pulses at 0% of rMT was applied at the very same position	WMFT, MESUPES, Finger tapping, MEP

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Luk 2022 [83]	12/12	10/14	67.3/65.1	1 month < stroke duration < 6 months /subacute	IS and HS	Mild to moderate weakness in the affected upper limb	rTMS + motor task practice	1200 pulses, 1 Hz, 90% of RMT, weekdays, 2 weeks, 10 sessions	A 70-mm Fig. 8 coil /contralesional M1	Sham rTMS Motor task practice: 30 min, twice weekly for another 10 weeks after the end of the initial 2-week treatment period	Sham stimulation was conducted by positioning the coil at an angle of 90° relative to the scalp instead of tangentially to the hotspot, but the coil produced the same sounds as in real rTMS	FMA-UL, MEP, grip force, ARAT, NHPT, BBT, RT, SIS
Lv 2023 [51]	54/18	32/30	57.6/57.8	18.5 days/acute	IS	Brunnstrom stage I–III, with muscle tone (modified Ashworth scale) less than 1 (not more than 1 + at the end of treatment)	rTMS + Conventional rehabilitation	A group: 1200 pulses, 1 Hz, 80% RMT, one session per day, 5 sessions per week, 2 weeks B group: 1200 pulses, 1 Hz, 80% RMT, one session per day, 5 sessions per week,4 weeks C group: 1200 pulses, 1 Hz, 80% RMT, one session per day, 5 sessions per week, 6 weeks	9 cm Fig. 8 coil/ contralateral M1	rehabilitation	DR	FMA-UE, WMFT, MEPs
Maclolm 2007 [84]	9/10	8/11	68.4/65.7	At least 1 year /chronic	IS and HS	At least minimal motor function in the paretic arm, as defined by Wolf et al	rTMS + constraint -induced therapy	2000 stimuli, 20 Hz, 90% RMT, 50 trains of 40 stimuli, stimulus, stimulus train duration of 2 s, with an intertrain interval of 28 s, daily, ten consecutive weekdays	-cm-diameter figure-8 coil/ affected M1	Sham rTMS Constraint-induced therapy (CIT) for upper-limb hemiparesis	Sham rTMS was administered using a specially designed Magstim figure-eight coil (Magstim Ltd, UK). This coil generates a magnetic field that is more than 90% attenuated, but it does produce noise and vibration comparable with those of a real magnetic coil. We simulated this muscle contraction (and concomitant cutaneous and intramuscular neural sensory input) during sham rTMS by attaching surface electrodes underneath the magnetic	WMFT, WMFT, MAL

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
											coils and in contact with the scalp connected to the electromyograph. During sham rTMS, we simultaneously administered a train of 20 Hz electrical impulses to the scalp. Stimulus parameters for sham rTMS were identical to those for real rTMS (i.e., 50 trains of 40 sham stimuli administered at a rate of 20 Hz with intertrain intervals of 28 secs)	
Matsuura 2015 [58]	10/10	9/11	72.2/74.7	Acute ischemic stroke (mean stroke onset is 9.6 days) /acute	IS	Mild to moderate motor impairment in one hand with a score equal to or less than 63 FMA and could extend at least 20°at the wrist for MRCP measurement	rTMS	1200 pulses, 1 Hz, 100% MT, 20 min, daily, 5 days	70-mm Fig. 8 coil /contralesional M1	Sham rTMS	Sham rTMS was performed by placing the coil perpendicularly to the scalp to reproduce the noise of a 1 Hz stimulus and tactile sensation on the scalp without cortical stimulation	FMA-UL, pegboard, grip strength, PPT
Mello 2015 [59]	9/9	9/9	57.1/51.1	5–45 days (mean stroke onset is 28.5 days) /acute	IS	Mild to severe hand paresis (MRC,4–0 in finger flexion or extension)	rTMS + PT	1500 pulses, 1 Hz, 90% RMT, 25 min, 5 days/week, 10 sessions	Figure 8 coil (mean diameter 70 mm) /contralesional M1	Sham rTMS Rehabilitation treatment, 60 min, 5 days per week, during 2 weeks (total, 10 treatment sessions)	In the sham intervention, the coil was held perpendicularly to the vertex	RMT, SICI, ICF
Meng 2017 [60]	10/10	3/17	64.8/65.2	DR	IS	DR	rTMS + Rehabilitation training	1800 pulses, 1 Hz, 90% MT, 30 min, daily, 14 days	70 mm Fig. 8 coil /contralateral M1	Sham rTMS Rehabilitation training: 40 min, twice a day	In the control group, patients were given 30 min of sham stimulation once per day. Patients were able to hear magnetic stimulator, but did not receive any real magnetic stimulation	NIHSS, BI, FMA

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Petruseviciene 2023 [52]	24/11	14/24	65.08/76	No more than 1 month /acute	IS	Muscle strength ≤ 4 points (as assessed by the Lovett scale)	rTMS + Conventional rehabilitation	HF group: 10 Hz, 80% RMT, 1200 pulses (30 trains, 40 pulses per train, intertrain interval 20 s). 10 rTMS sessions over 2 weeks LF group: 1 Hz, 80% RMT, a total of 1200 pulses (10 trains, 120 pulses per train, intertrain interval 20 s) 10 rTMS sessions over 2 weeks	"8" coil HF: ipsilesional M1 LF: contralesional M1	Rehabilitation	DR	Unaffected upper extremity hand grip strength; Affected upper extremity hand grip strength; FIM
Qin 2021 [61]	23/18	16/25	58.5/62.3	1–3 months/subacute	IS	DR	rTMS + Rehabilitation training	1200 pulses, 1 Hz, 90% MT, 10 pulses with 2 s interval, once a day, 5 days/week, 8 weeks	Air-cooled Fig. 8 coil /contralateral M1	Sham rTMS Routine rehabilitation training and neurodevelopmental therapy, 40 min, once a day, 5 days/week, 8 weeks	The sham stimulation group underwent rTMS with the same parameters (including position, stimulation frequency, interval time, and pulse number) as the LF-rTMS group. However, during intervention, the coil was inverted on the surface of the skull to ensure that it had the same stimulation sound without any effective stimulation	FMA-UL, MBI
Qin 2023 [62]	15/14	9/20	55.9/59.4	1 and 6 months /subacute	IS	Upper limb Brunnstrom recovery period of 3–5, upper spasticity MAS score of 1–3	rTMS + rehabilitation training	1 Hz, 90% RMT, 1200 pulses Ten pulses with an interval of 2 s, once a day, 5 days a week, 8 weeks	Air-cooled Fig. 8 coil/contralateral M1	Routine rehabilitation training, 40 min, 5 days a week, 8 weeks	NA	FMA-UL, MBI, MAS, amplitude of low-frequency fluctuation (ALFF)
Rastgoo 2016 [85]	10/10	4/16	54.6/49.7	≥ 6 months /chronic	IS and HS	Ability to walk independently (with or without walking aids)	rTMS	1000 pulses, 1 Hz, 90% MT, 20 min, five consecutive daily sessions	Figure of eight coil (diameter of each wing, 90 mm)/ unaffected M1	Sham rTMS	For the sham stimulation, the coil held over the unaffected LE motor area as for active stimulation but with application of an audio coil, no magnetic stimulation was delivered to the brain	MMAS, Hmax/Mmax ratio, TUGT, FMA-LL

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Revill 2020 [63]	11/11	11/11	59.8/63.5	More than 6 months /chronic	IS	DR	rTMS + hand motor training	0.1 Hz, 80% MT, 5 consecutive days	Air-cooled figure of eight coil (7-cm wing diameter) /ipsilesional M1	Sham rTMS Hand motor training, 30 min, five consecutive days	Sham stimulation was applied through an air-cooled sham coil, which mimics the experience of subthreshold stimulation with the real coil	Jebsen Taylor Test
Rezaei 2023 [103]	10/10	9/11	50.50/53.9	Within 1 to 6 months/subacute phase of stroke	DR	Score of 22–44 on the Fugl-Meyer assessment for upper extremity (FMA-UE)	rTMS + PT	20 Hz, 5 s, intertrain interval for 50 s, 20 trains, 2000 pulses at 90% RMT, 10 treatment sessions, three times per week	70-mm figure-8 coil/ipsilesional M1	PT,10 sessions, 3 times per week	DR	FMA-UE, BBT, grip strength, pinch strength
Sasaki 2017 [86]	11/10	8/13	66.5/62.4	Within 6 h /acute	IS and HS	DR	rTMS + Conventional rehabilitation	1000 pulses, 10 Hz, 90% RMT, 10-s trains with 50-s intertrain intervals, 10 min, daily, 2 sessions, 10 days	-mm double-cone coil/bilateral leg motor areas	Sham rTMS Conventional rehabilitation: 40–80 min, daily, 10 min, daily, 2 sessions, 10 days, medical treatment	Sham stimulation was performed with a pseudo-coil that was not connected to the stimulator. Patients in the sham group received only recorded sounds of 10-Hz stimulus from a speaker for 10 min	BRS, ABMS II
Sasaki 2013 [87]	20/9	9/20	67.3/63.0	Within 6 h /acute	IS and HS	No disturbance of consciousness (a score of eye opening of 4 and best verbal response of 5 on the GCS	rTMS + Conventional rehabilitation	HF group: 1000 pulses, 10 Hz, 90% RMT, 10-s trains with 50-s intervals, 10 min, daily, 5 days LF group: 1800 pulses, 1 Hz, 90% RMT, 30 min, daily, 5 days	70-mm Fig. 8 coil /HF: ipsilesional M1 LF: contralesional M1	Sham rTMS Conventional rehabilitation: 40 to 80 min each day from 3 days on average after onset Conventional medical treatment	Sham stimulation was performed with the coil held at an angle of 90 to the scalp to reproduce the noise of 1-Hz stimulus for 10 min	grip strength, tapping frequency
Sengul 2023 [88]	24/13	29/8	61.2/57	≥ 12 months /chronic	IS and HS	Grade 2 or 3 muscle tone/spasticity according to MAS in at least one of the upper-limb muscle groups	rTMS	LF group: 1500 pulses, 90% RMT, 1 Hz, 25 min, single-session HF group: 1500 pulses, 90% RMT, 10 Hz, 5 s stimulation, 25-s interval, 30 min, single session	Figure 8 coil /contralesional dorsal premotor (the site 2.5 cm anterior to the motor "hot spot" area of the first dorsal interosseous (FDI) muscle)	Sham rTMS	The sham stimulation was performed by holding the probe of the device perpendicular to the vertex. The device was operated without actual stimulation at the lowest operating power of 1 to produce the same sound and warning sounds as in the inhibitory rTMS application	MAS, F/M amplitude ratio,

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Seniow 2012 [98]	20/20	14/26	63.5/63.4	≤ 3 months /subacute	IS and HS	Moderate paresis of the affected upper extremity of the affected upper extremity (NIHSS—motor arm score of 1 to 3)	rTMS + individual physiotherapy	1800 pulses, 1 Hz, 90% RMT, 30 min	Air-cooled Fig. 8 coil (each loop 70 mm in diameter) /contralesional M1	Sham rTMS Individual physiotherapy 45 min, daily, 5 days per week for 3 weeks	Sham stimulation was performed with a coil that imitates the sound of a real TMS coil. The stimulation parameters were chosen in accordance with the current safety guidelines for rTMS	WMFT, FMA, NIHSS
Sharma 2020 [64]	47/49	29/67	54.9/52.9	Within the last 15 days /acute	IS	NIHSS of 4–20	rTMS + Conventional physical therapy	750 pulses, 1 Hz, 110% RMT, 75 trains, 45 s ITI, daily, 5 days/week, 2 weeks, 10 sessions	Air-cooled figure of 8 coil (70 mm) /contralesional M1	Sham rTMS Conventional physical: 45-min conventional physical therapy, 90 ± 7 days post-recruitment	Sham rTMS pulses were administered using the same stimulation parameters	MBI, FMA-UL, FMA-LL, Hamilton Depression, MRS, NIHSS
Shim 2023 [38]	14/16	12/18	67.3/63.6	Within 6 months(mean stroke onset is 3.3 months) /subacute	DR	Motor defects in the damaged upper extremities	rTMS + motor learning group	80% RMT, 10 Hz for 2 s, ITI 58 s, 200 times, 10 min, three times a week, 4 weeks	70-mm, 8-shaped coil/M1 affected	Sham rTMS combined with the motor learning, 10 min, three times a week for 4 weeks	Sham rTMS provided a small intensity of 2% of the RMT that could not cause excitement in the motor cortex but was set to the same frequency of noise as the HF-rTMS	FMA-UL, BBT, force gauge, K-MBI,
Shu 2024 [93]	30/30	26/34	67/62	15 days of onset and within 6 months	IS and HS	Lower limb Brannstrom staging ≥ stage II; disease course ≥ 2 weeks; standing balance ≥ level 1	rTMS + Conventional rehabilitation	1 Hz, high-intensity stimulation of 100% motor threshold using selected treatment devices. Each stimulation lasted for 20 min, once a day, consecutively for 2 weeks, with 5 days per week, a total of 10 times	"∞" shaped coil/ contralesional M1	Routine medication	DR	Stride speed(cm/s), Stride frequency(step/min), Stride length (cm), Stride width(cm), Affected side stride length, Affected side gait period, affected joint motion angle, affected side dynamic parameters, gait parameters

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Takeuchi 2005 [65]	10/10	5/15	58.4/59.6	≥6 months /chronic	IS	DR	rTMS + pinching task	1 Hz, 90% RMT, 25 min, once	70-mm Fig. 8 coil /contralesional M1	Sham rTMS Pinching task: 60 min interrupted by a 15-min break to rest after 30 min and pinching task for 15 min per day for 7 days from the day after the end of practice 1 until the day before the rTMS procedure	Sham stimulation was given positioning the coil perpendicularly to the scalp of the contralesional M1 at the same frequency and intensity as real rTMS	RMT, MEP, Pinch force,
Takeuchi 2008 [66]	10/10	4/16	61.2/63.4	More than 6 months / chronic	IS	Patients could perform a pinching task	rTMS + motor training	1500 pulses, 90% RMT, 1 Hz, 25 min, once	70-mm Fig. 8 coil /contralesional M1	Sham rTMS Motor training, 15 min	Sham stimulation was applied over the unaffected hemisphere by positioning the coil perpendicular to the scalp and at the same frequency and intensity used for real rTMS	acceleration and pinch force
Tosun 2017 [67]	9/9	7/11	57.6/61.3	<6 months /49 days /47 days /subacute	IS	Minimum 10° of volitional flexion and extension of fingers and wrist in the affected limb	rTMS + PT	1200 pulses, 1 Hz, 90% RMT, 20 min, 5 days/week, 10 sessions, 2 weeks	Figure 8 coil /contralesional M1	PT + OT: daily, 5 days/week, 4 weeks, 20 sessions	NA	BRS, FMA-UL, BI, MAS
Wang 2014 [89]	30/14	10/34	62.7/68	3 to 12 months (mean stroke onset is 6.7 ± 3.2 months) /chronic	IS and HS	The early Brunnstrom stage (I–IV)	rTMS + PT + OT	cM1 group: 600 pulses, 1 Hz, 90% RMT, 5 stimuli at 10-s intervals, daily, 10 sessions cPMd group: 600 pulses, 1 Hz, 90% RMT, 5 stimuli at 10-s intervals, daily, 10 sessions	70-mm figure-8 coil /cM1 group: contralesional M1 /cPMd group: contralesional PMd (3 cm anterior to the M1 cortex)	Sham rTMS PT: 1 h, daily, 3 times per week OT: 1 h, daily, 2 times per week, alternated with physical therapy	A sham group underwent sham stimulation of the cM1 through the use of a placebo coil (Magstim Co) and was subjected to procedures identical to those applied to the cM1 group. The conditioning protocol administered to the sham group was identical to that administered to the cM1 and cPMd groups, except no conditioning current was generated	FMA-UL, WMFT, MRC

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Wang 2022 [90]	38/20	23/35	55.8/55.9	Within 2 weeks to 3 months (mean stroke onset is 8.2 weeks) /subacute	IS and HS	DR	rTMS + Conventional rehabilitation	HF group: 5 Hz, 2 s per session, intertrain interval 8 s, 90% RMT, 18 min, daily, 21 days LF group: 1 Hz, 15 s, intertrain interval 2 s, 90% RMT, 18 min, daily, 21 days	7-cm figure-8 circular coil /HF: contralesional M1/ LF:contralesional M1	Sham rTMS Rehabilitation treatment, 25 min twice a day, 21 days	The sham group received rTMS with the same parameters (noise, time, and frequency) as the 1 Hz rTMS group over the unaffected hemisphere but with the coil rotated 90o away from the scalp so that minimal current was induced in the brain	FMA-UL, WMFT, MBI
Wang 2024 [94]	27/25	33/19	60.95/61.76	Onset of stroke ranged from 14 to 45 days/12.37D/16.42D/ Acute	IS and HS	The Bruininks—Oseretsky Test (BOT) for lower-limb staging shows stages 2 or 3	rTMS + Conventional rehabilitation	1 Hz, 90% RMT, each sequence lasts 10 s with a 5-s interval, and this is repeated for 60 sequences, totaling 15 min and 600 pulses. 15 min per session, once a day, and 5 days a week for 6 weeks	"8"-shaped coil/ contralesional M1	Sham rTMS	Parameters are the same as LF-rTMS. The coil oriented perpendicular to the cranial bone surface	FMA-LL, BBS, MBI
Wang 2020 [91]	30/15	15/30	59.6/60.5	14–90 days (mean stroke onset is 28.5 days) /acute	IS and HS	FMA score < 50/100 with severe motor impairment	rTMS + Conventional rehabilitation	HF group:1000 pulses, 10 Hz, 100% RMT, 1 s per session, 10 s interval, 100 sessions per treatment, daily, 14 days LF group:1000 pulses, 1 Hz, 10 s, 30-s interval, 100 sessions per treatment, daily, 14 days	Figure 8 coil with a 90-mm diameter /contralesional M1	Sham rTMS Conventional physical rehabilitation and occupational therapy, lasting 40 min, one session per day	Sham rTMS applied over the contralesional M1 before physiotherapy daily for two weeks	FMA, RMS-SEMG, BI, MEP, CMCT
Wang C 2023 [68]	80/160	83/157	63.9/64.1	≤ 2 months/21.32D/21.25D /21.42D/acute	IS	DR	rTMS + routine rehabilitation	HF: 10 Hz, 15 min, once a day, 6 days a week, 3 weeks LF: 0.5 Hz, 40 min each time, once a day, 6 times a week, 3 weeks	Did not reported type of coil/HF: ipsilateral M1 /LF: contralateral M1	Sham TMS Routine rehabilitation: 3 weeks, 6 days a week, 120 min per day	The sham stimulation group was given sound stimulation at the same frequency as the high-frequency group in the M1 area of the central anterior gyrus of the cortex on the lesion side. 3 weeks, 6 times/ week, 15 min/time	NIHSS, MRS, FMA, BBS, MBI, MEP cortical latency, CMCT
Wang T 2023 [99]	23/23	13/33	62.2/61.8	101 days /91 days /subacute	IS and HS	Severe upper limb /Brunnstrom approach stage ≤ 3 and a FMA score below 50	rTMS + Conventional rehabilitation	90% RMT, 1 HZ, 10 s followed by a 2-s pause, 20 min, daily, 14 days	-shaped coil/ contralateral M1	Rehabilitation treatment, once a day, 2 consecutive weeks	NA	FMA-UL, MBI

Table 2 (continued)

ID	No. of participants (Exp/Ctr)	Gender (F/M)	Mean Age, Y(Exp/Ctr)	Stroke duration	Type of stroke	Severity of stroke	Intervention of experimental group	rTMS Protocol	Coil/position	Intervention of control group	Method of Sham rTMS	Outcomes Measure
Wu 2023 [100]	15/15	8/22	57/55.3	2 weeks to 6 months (mean stroke onset is 33 days) subacute	IS and HS	Upper limb dysfunction and Brunnstrom stage I-III of the affected upper limb	rTMS + conventional rehabilitation therapy	10 Hz, 80% RMT, 1000 pulses, daily, five times per week for 3 weeks	95-mm focal Fig. 8 coil /ipsilateral M1	Sham rTMS + conventional rehabilitation therapy (30 min of PT and a 30 min of OT, twice per day, five times per week for 3 weeks.)	The coil was held at an angle of 90o to the hotspot so that patients could hear the sound but no actual stimulation effect	FMA-UL, WMFT, MBI, Brunnstrom motor recovery stage of the upper extremity and hand
Yang 2021 [101]	26/13	11/28	62.4/64.0	1 to 6 months /subacute	IS and HS	Brunnstrom of hemiplegic upper limb and hand staging from 4 to 5/mild motor dysfunction	rTMS + Conventional rehabilitation	750 pulses, 5 Hz, 100% RMT, 5 min, 5 days/week, 2 weeks	90-mm Fig. 8 coil /contralateral M1	Sham rTMS PT + OT: 120 min, daily, 10 sessions, 5 days/week for 2 weeks	The sham stimulation was conducted with the coil placed rotated 90o away from the scalp resulting in no current generated in the brain	JTHFT, FMA-UL, grip strength, MBI, iMEP
Yu 2022 [102]	9/9	3/15	54.6/57.4	≤3 months (mean stroke onset is 1.18 months) /subacute	IS and HS	Ability to walk more than 10 m independently	rTMS + conventional physical + medical treatment	1200 pulses, 5 Hz, 80% RMT, 5 days/week, 2 weeks	"8" coil /surface of the scalp of the left dorsolateral prefrontal cortex (DLPFC)	Sham rTMS Rehabilitation, 45 min	The coil was placed vertically in the sham group	MoCA, FMA-LL,10MWT, BBS, TUGT, SCWT, Gait analysis, plantar pressure parameters
Xie 2023 [95]	47/21	23/45	56.27/61.76	61D	IS and HS	Presence of mild, moderate or severe unilateral motor dysfunction	rTMS	LF: 1 Hz, 600 s, 600 pulses of intervention HF: 5 Hz, 2 s, intertrain interval 4 s, 100 trains	LF: contralesional M1 HF: ipsilesional M1	Sham rTMS	The sham group used the same parameters as	The HF-rTMS group. However, the regular coil was kept at 90

IS ischemic stroke, *DR* Do not report, *PT* physical therapy, *RMT* resting motor threshold, *M1* primary motor cortex, *NA* Not Applicable, *BRS* Brunnstrom Recovery Stages, *FMA-UL* Fugl-Meyer Assessment for upper limb, *FMA-LL* Fugl-Meyer Assessment for lower limb, *BBT* Box and Block test, *MAS* Modified Ashworth Scale, FIM, Functional Independence Measurement; MMSE, Mini-mental Status Examination; FAS, Functional Ambulation Scale; HS, hemorrhagic stroke; JHFT, Jebsen-Taylor Hand Function Test; NHPT, Nine-Hole Peg Test; ROM, range of motion; SSQOL, stroke-specific quality-of-life scale; *SSQOL-UE* upper-extremity stroke-specific quality-of-life scale, *RP* the number of responsive points, *AM* amplitude, *MRP* motor relearning procedure, *FMA-BL* Fugl-Meyer Assessment balance function score, *MRS* Modified Rankin Scale, *LF* Low frequency, *HF* High frequency, *APB* abductor pollicis brevis, *FMA* Fugl-Meyer Assessment, *BI* Barthel Index, *10MT* Ten-meter walking test, *6MWT* Six-min walking test, *MRC-UL* upper limb score of Medical Research Council score, *MRC-LL* lower limb score of Medical Research Council score, *NIHSS* National Institutes of Health Stroke Scale, *MRC* Medical Research Council scale, *fMRI* functional magnetic resonance imaging, *AMT* Active Motor Threshold, *NHISS* National Institute of Health stroke scale, *EQ-5D* EuroQol Five Dimensions Questionnaire, *cRMT* contral-lesion resting motor threshold, *iRMT* ipsi-lesion resting motor threshold, *FT-r* paretic-to-contralateral ratio, *AI* AI scores, *cRT* choice reaction time, *PPT* Purdue Pegboard test, *WMFT* Wolf Motor Function Test, *ARAT* Action Research Arm Test, *SIS* Stroke Impact Scale, *PHQ-9* Patient Health Questionnaire-9, *OT* occupational therapy, *TUGT* Timed Up and Go Test, *MMT* manual muscle test, *PASS* Postural Assessment Scale for Stroke, *POMA-b* balance subscale of the Tinetti Performance Oriented Mobility *Assessment, MEP* motor evoked potential, *SSQOL* Stroke Specific Quality of Life Scale, *ITI* inter-train intervals, *SSS* Scandinavian Stroke Scale, *BBS* Berg Balance Scale, *10MWT* 10-m walk test, *K-MBI* Korean version of Modified Barthel Index, *FAC* functional ambulation classification, *MT* motor threshold, *MESUPES* Motor Evaluation Scale for Upper Extremity in Stroke Patients, *NHPT* nine-hole peg test, *MAL* Motor Activity Log, *MRCP* Movement-related cortical potential, *MMAS* modified Ashworth scale, *GCS* Glasgow Coma Scale, *cM1* contralesional M1, *cPMd* contralesional premotor cortex, *RMS-SEMG* root mean square of surface electromyography, *CMCT* central motor conduction time, *iMEP* ipsilesional motor evoked potential. *ABMS II* Ability for Basic Movement Scale Revised

pinching tasks, and constraint-induced therapy, augmented reality gait adaptive training, and augmented reality gait adaptive training. The types of TMS coils used in these studies included 8-figure collars, H-type coils [80], double-cone coils. One trial did not report the type of coil used [44]. The frequencies used in rTMS included 0.1 Hz, 0.5 Hz, 1 Hz, 3 Hz, 5 Hz, 10 Hz, and 20 Hz. The coil was positioned over the primary motor cortex (M1) in 58 studies, over the dorsal premotor cortex (PMd) (located 3 cm anterior to the M1 cortex) in one study [89], over the surface of the scape of the left dorsolateral prefrontal cortex (DLPFC) in one study [102], 2 cm below the inion and 2 cm lateral to the midline on the cerebellar hemisphere ipsilateral to the ataxic side, with the handle pointing superiorly, targeting the posterior cerebellar lobe in one study [57], and over the dorsal premotor (the site 2.5 cm anterior to the motor "hot spot" area of the first dorsal interosseous (FDI) muscle) in one study [88]. Specifically, in a total of 55 studies employing 1 Hz rTMS, the stimulation site was the contralateral M1. Four studies utilized 3 Hz rTMS, with two studies stimulating the contralateral M1 and two studies stimulating the ipsilesional M1. Furthermore, eight studies employed 5 Hz transcranial magnetic stimulation, with five studies stimulating the ipsilesional M1, two studies stimulating the ipsilesional M1, and one study stimulated the DLPFC. Ten studies utilized 10 Hz rTMS, with three studies stimulated the contralateral M1, five studies stimulated the ipsilesional M1, one study stimulated the bilateral leg motor areas, and one study stimulated the FDI. The three studies employing 20 Hz rTMS stimulated the ipsilesional M1. The intensity of stimulation varied between 200 and 7500 pulses. The times of intervention sessions ranged from twice per week to six times per week, whereas the total number of intervention sessions ranged from one to 40 sessions. Two studies employed the active motor threshold (AMT) to determine intervention intensity [45, 78], whereas other studies used the resting motor threshold (RMT). The intervention intensity used in the two AMT studies was set at 120% AMT and 90% AMT. The intervention intensity in the other studies varied from 80 to 120% of RMT. The duration of each intervention varied between 2 and 30 min. Thirty-three studies conducted interventions without any subsequent follow-up [35, 38–40, 45, 46, 51, 58–62, 65, 67, 71, 73, 74, 79, 84, 86, 87, 89–91, 93–97, 99, 101–103]. The remaining studies had follow-up periods ranging from 7 days to 18 months.

(3) Comparison

Among the 68 studies included, nine studies compared rTMS with sham rTMS [41, 48, 58, 72, 80, 85, 88, 94, 95], whereas sixteen studies compares rTMS with rehabilitation [37, 39, 40, 45, 51, 52, 62, 67, 71, 74, 92, 93, 96, 97, 99, 103]. Additionally, other studies compared rTMS with a combination of sham and rehabilitation. The rehabilitation interventions included physical therapy (PT), occupational therapy (OT), motor task practice, hand motor training, pinching task, and conventional rehabilitation, augmented reality gait adaptive training, and augmented reality gait adaptive training.

(4) Outcome

Motor function was assessed using a variety of measures, including the FMA, FMA-UL, FMA-LL, MAS, Box and Block test (BBT), Brunnstrom Recovery Stages (BRS), range of motion (ROM), ten-meter walking test (10MT), six-min walking test (6MWT), Jebsen-Taylor Hand Function Test (JHFT), RMT, grip strength, Pegboard Tasks, Ankle dorsiflexion, Hip flexion, Berg Balance Scale (BBS), Action Research Arm Test (ARAT), Postural Assessment Scale for Stroke (PASS), balance subscale of the Tinetti Performance Oriented Mobility (POMA-b), Wolf Motor Function Test (WMFT), TUGT, and pinch strength. The assessment of ADLs involved the utilization of the Modified Barthel Index (MBI) and Barthel Index (BI). Additionally, the evaluation of quality of life involved the use of various instruments, such as NHISS, Stroke Impact Scale (SIS), Stroke Specific Quality of Life Scale (SSQOL), and Euro-QoL Five Dimensions Questionnaire (EQ-5D).

Methodological quality of the studies

The risk of bias summary for the included studies is presented in Fig. 2. Among the included studies, twenty-eight trials did not provide information on randomization allocation [36, 41, 43, 45, 48, 55, 58, 60–63, 65, 66, 72, 74, 76, 78–81, 84, 85, 87, 91, 95, 98, 100, 103]. As a result, these studies were evaluated as having an "unclear" risk of bias concerning the "Random Sequence Generation (Selection Bias)" criterion. In contrast, forty-one studies reported employing various randomization methods, such as sealed envelopes [28, 35, 46, 47, 50, 54, 56, 57, 82, 83, 89, 99], blank-coded magnetic cards [80], random number computerized generator [37, 39, 40, 42, 44, 49, 51, 53, 59, 67, 69, 73, 75, 77, 88, 90, 92–94, 96, 97, 101], website [70], tables of random number [68, 71, 102], and simple random sampling method [38, 38]. These studies were identified as having a "low" risk of bias in the "Random sequence generation (selection bias)" category. One trial, which assigned patients based on the date of admission, was identified as having a high risk of bias [86]. A total of twenty-three studies provided information regarding the concealment of allocation, employing methods such as sealed envelopes [28, 35–37, 43, 46, 47, 49, 50, 54, 56, 57, 64, 73, 82, 88, 89, 97, 99], locked cabinet [42],

Table 3 Characteristics of included studies in this systematic review (continue)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Abdelkader 2024 [92]	DR	DR	Yes	No one
Aşkın 2017 [40]	DR	DR	No	No one
Avenanti 2012 [69]	DR	DR	No	DR
Barros 2014 [70]	DR	No adverse events were reported by any of the participants	No	Two patients (1 in each group) dropped out after the post-intervention evaluation, leaving 18 participants who completed all the study procedures
Blesneag 2015 [41]	The region of MCA	DR	No	No one
Chen 2023 [71]		DR	No	DR
Chervyakov 2018 [35]	The region of MCA	Two patients developed secondary generalized epileptic seizures. One female patient presented with seizures during single-pulse stimulation for diagnostic mapping. Nine patients withdrew from the study at different stages because they developed epileptic seizures, reported subjective "bad" or "tired" feelings after rTMS session(s) or for no cause. Thirteen participants were excluded from analysis, mainly because of incomplete data sets	No	Nine patients withdrew from the study at different stages because they developed epileptic seizures, reported subjective "bad" or "tired" feelings after rTMS session(s) or for no cause
Chieffo 2021 [80]	DR	No serious adverse events were reported. Vital signs remained stable after treatment for all participants. Three subjects reported transitory dizziness, and one showed muscle twitches on shoulders during real rTMS. For these patients, intensity was lowered to a comfortable level (80% of RMT on average), and all subjects completed the whole treatment cycle	No	One subject (Subject 9 Table 1) attended all sessions of the first treatment but withdrew from the protocol before the second phase for personal reasons
Conforto 2012 [42]	The region of MCA	There were no serious intervention-related adverse events. There were no significant differences in rates of sleepiness (86.7%, active and 78.6%, sham; local or nuchal pain (33.3%, active and 28.6%, sham; = 0.46; sham group, = 0.65) or headache, = 1.0) between the groups. Head or nuchal pain were mild and subsided spontaneously after a few minutes.	No	1 drop off because recurrent stroke

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
		None of the patients reported dizziness or paresthesias. No syncopes or seizures were observed. There were no significant differences in systolic (active group, blood pressure (active group, = 0.76; sham group = 0.21) or diastolic = 0.26; sham group = 0.96), and heart rate (active group = 0.32), along the ten sessions of treatment		
Du 2016 [36]	The region of MCA	No adverse effects were observed except for three transient headaches and one tingling sensation on the head at the beginning of the stimulation	No	7 of experimental group lost,1 of control lost
Du 2019 [43]	The region of MCA	Fifty-three patients successfully completed the intervention protocol with no adverse effects, except for two transient headaches at the beginning of stimulation (both in HF-rTMS groups)	No	6 of experimental group lost,3 of control lost
Edwards 2023 [47]	Cortical/Subcortical/Cortical/subcortical/Brainstem	Ten serious unrelated adverse events occurred (4 active group, 6 sham group, $P = 0.72$)	Yes	3 lost in rTMS group, and 1lost in sham group
El-Tamawy 2019 [45]	DR	DR	No	DR
El-Tamawy 2020 [46]	the region of MCA	DR	No	DR
Emara 2010 [47]	DR	No significant adverse events were observed during treatment in either group. Six patients (four active rTMS and two controls) experienced transient headache or tingling sensation in the head following the rTMS session. This resolved spontaneously within 30 min in three patients and required oral paracetamol in the other three to effectively control the symptoms	No	DR
Fang 2024 [96]	DR	One patient reported a mild headache during rTMS, which subsided once the intervention stopped	No	4 patients drop out
Forogh 2017 [72]	DR	DR	No	11 patients (5 patients in the treatment and 6 patients in Sham group) withdrew from the study

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Fregni 2006 [48]	Left basal ganglia Left internal capsule Left putamen Left internal capsule Left corona radiata Left internal capsule (posterior limb) Left internal capsule Right lentiform nucleus Right internal capsule Left somatosensory cortex Right frontal lobe Left temporofrontal Left putamen and caudate Left corona radiata Left putamen	There were few adverse events. In the active group, one patient reported a mild headache (contralateral to the side of TMS application) and one patient reported an increase in anxiety. In the sham rTMS group, one patient reported an increase in the tiredness and one patient reported a mild headache	Yes	There were no dropouts and the few missing data were considered missing at random
Gong 2021 [37]	The region of MCA	Except for two transient headaches on the head at the beginning of the stimulation, no adverse effects were observed in this study, such as seizures	No	2 patients drop off
Gottlieb 2021 [73]	The region of MCA	Five patients reported a mild adverse event within 24 h after the rTMS session (headache: $n=4$, pain in contralateral hand: $n=1$). One patient with headache needed a low dose of an analgetic. However, the frequency of reported adverse events was equal in both groups	No	Six patients did not receive complete intervention and one patient of the sham-rTMS group had to be excluded from the analyses because the second examination could not be performed
Guan 2017 [49]	The region of MCA	None of the patients complained of discomfort after rTMS or sham rTMS	No	8 patients in the treatment group and 7 patients were lost to follow- up due to personal reasons
Haghighi 2021 [74]	The region of MCA	All participants completed the study protocol without any adverse events	Yes	The treatment and assessment sessions were completed by all the participants
Harvey 2018 [75]	Cortex, subcortical, both cortex and subcortex, brain stem, centrum semiovale, corona radiata, basal ganglia, internal capsule, and thalamus	Of the safety population ($n=196$), a total of 26 serious adverse events occurred in 18 participants. Rates within treatment arms were not significantly different. The most common treatment-related adverse events were arm and hand pain, spasm or myalgia ($n=14$), head discomfort ($n=11$), and paresthesia ($n=6$). These were transient and resolved within 24 h of onset	Yes/Missing values were imputed using the last observation carried forward principle	Because of 3 participants withdrawing before study interventions, the safety sample is 196. The per-protocol sample was 169 after removing 30 subjects with significant protocol deviations (15 active and 15 sham)

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Higgins 2013 [76]	DR	Did not experience adverse events related/No subjects reported experiencing headaches or any sort of discomfort following the rTMS or the behavioral intervention	Yes	Of the eleven subjects recruited, two subjects withdrew from the study before the post intervention evaluation. One withdrew following an adverse event during but not related to the intervention session. The subject experienced an important drop in blood pressure, having taken the wrong dose of medication on the morning of the treatment. He had completed five intervention sessions. The second participant withdrew following four intervention sessions. She had sustained a fall at home and was no longer able to travel for the study
Hosomi 2016 [77]	Subcortex and Involvement of cortex	There were no serious adverse effects observed during or after the stimulations during the 2-week follow up period after completion of stimulations. As was previously mentioned, 1 subject withdrew from the protocol due to uncomfortableness. Incidentally, he later apparently demanded continuation of stimulations, after which he reportedly found the same stimulation pattern relaxing and enjoyable	No	Two subjects in the real stimulation group failed to complete the study. One patient did not like the stimulation sensation on the scalp after one 10-s train of stimulations on the first day of stimulations, and declined following stimulations. The other patient also temporarily refused other forms of treatment such as regular rehabilitation during the first week of the stimulation
Huang 2018 [78]	Cortical involved subcortical only	DR	No	Four patients withdraw
Jia 2024 [97]	DR	No adverse events were observed during the intervention period	No	Two patients were discharged early, one patient refused treatment, and one patient withdrew from treatment because of a recurrence of cerebral hemorrhage
Juan 2022 [50]	The region of MCA	DR	No	Fourteen patients dropped out during the trial for different reasons, mainly symptom exacerbation, incompliance or poor fMRI data quality
Ke 2020 [53]	Cortex and subcortex	Because of medical insurance complications, leading to rTMS termination. In addition, four patients were lost during follow-up: two patients in the sham group and one patient in each of the short and long ITI rTMS groups	No	Four patients (one from the sham group, two from the short ITI group, and one from the long ITI group) were discharged before the end of rTMS. because of medical insurance complications, leading to rTMS termination. In addition, four patients were lost during follow-up: two patients in the sham group and one patient in each of the short and long ITI rTMS groups

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Khedr 2005 [55]	Cortical/subcortical/massive	All patients completed the protocols, and there were no side effects of rTMS except occasional mild headache	All patients completed trail	All patients completed the protocols, and there were no side effects of rTMS except occasional mild headache
Khedr 2009 [54]	Ischemic stroke of middle cerebral artery territory/cortical and subcortical	All the patients tolerated rTMS well without any adverse effects	All the patients tolerated rTMS well without any adverse effects	All the patients tolerated rTMS well without any adverse effects
Khedr 2010 [56]	The region of MCA	All the patients tolerated rTMS well without any adverse effects	All the patients tolerated rTMS well without any adverse effects	Ten patients out of the 48 patients (four from the first group, three from the second group and three from the sham group) did not complete the follow-up at the end of the year. Four of them developed another stroke, two died before the end of the year and four could not attend because of family reasons
Kim 2014 [57]	Ischemic cerebellar or brain stem stroke with symptoms of ataxia (Cerebellum Pons Medulla)	Adverse events were not reported during and after the rTMS session in both real and sham rTMS groups	Yes	Two patients in the real rTMS group and 4 in the sham rTMS group were lost to follow-up for reasons not related to the intervention
Kim 2020 [28]	Cortical Subcortical Cortical/subcortical Brain stem	A total of 111 adverse events occurred in 48 participants and were more numerous among real rTMS: Most of the events were mild in real rTMS and 38 in sham rTMS) and only one serious adverse event (ischemic stroke recurrence) occurred in real rTMS but was determined to be unrelated to the intervention. There were 7 adverse device events for real rTMS and 2 for sham rTMS, with no statistically significant difference. No serious and unexpected ADEs were noted	Yes	One participant in the real rTMS group did not receive the intervention due to consent withdrawal. Three in the real rTMS group were lost to follow-up due to consent withdrawal before EOT. At 1 month after EOT, one participant from each group withdrew their consent
Lin 2015 [79]	DR	A Group E patient reported dizziness, and a Group C patient reported tingling scalp pain after the intervention sessions. These symptoms were tolerable and subsided after the treatment sessions	No	One patient was transferred to another hospital for personal reasons before treatment completion
Liang 2023 [39]	DR	DR	Yes	No one
Long 2018 [81]	In the territory of the middle cerebral artery or supratentorial intracerebral hemorrhage (ICH) without invasion into the cerebral cortex	No patient complained of pain or discomfort immediately after rTMS or during the follow-up visits. No patient experienced any pathologic symptoms, such as seizure or deterioration of motor function in the upper limb	No	All patients completed the protocols

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Ludemann-Podubecka 2015 [82]	The region of MCA	Participants tolerated the interventions well without serious adverse events	No	No one
Luk 2022 [83]	DR	The participants did not report any adverse events during the study period	Intention-to-treat analysis was first conducted. Any missing data would be substituted using the last-observation-carried-forward method	One participant from each group withdrew during the course of the study
Lv 2023 [51]	DR	DR	Yes	No one
Maclolm 2007 [84]	Middle cerebral artery, hemispheric lacunar infarcts, deep hemispheric hemorrhage, lacunar infarcts	There were no discernible adverse effects of rTMS beyond scalp discomfort	Yes	All patients completed study
Matsuura 2015 [58]	Subcortical stroke	All patients completed their rTMS sessions and did not report any adverse effects	No	All patients completed their rTMS
Mello 2015 [59]	Involving up to 50% of the internal carotid artery territory	In the active group, two patients reported headache or local pain (22.2%), two patients reported nuchal pain (22.2%), and five patients reported drowsiness (55.6%). In the sham group, three patients reported headache or local pain (33.3%), four patients reported nuchal pain (44.4%), and six patients reported drowsiness (66.7%)	No	One patient in the sham group had a recurrent stroke on the day before the second session of treatment and did not complete the study. Due to technical problems (malfunction of the paired-pulse TMS stimulator), cortical excitability data in 7 patients in the active group and 7 patients in the sham group were not collected. One patient in the active group coughed repeatedly during one of the TMS experiments
Meng 2017 [60]	Cerebral infarction of the internal carotid artery that was diagnosed based on clinical symptoms and signs	None of the patients had any severe adverse reactions such as recurrent stroke or seizures. One individual in the low frequency rTMS group experienced dizziness, but the symptoms disappeared soon after treatment	No	All patients completed study
Petruseviciene 2023 [52]	DR	DR	Yes	No one
Qin 2021 [61]	Subcortical stroke	DR	No	1 patient of real TMS and 6 patients of sham TMS did withdraw
Qin 2023 [62]	The middle cerebral artery territory	DR	No	2 patients drop off
Rastgoo 2016 [85]	Cortex Subcortex Both cortex and subcortex	No adverse events were reported by any of the patients throughout the study	DR	DR
Revill 2020 [63]	Ischemic infarction affecting M1 and/or corticospinal tract	DR	No	1 patient lost to follow-up because subject declined TMS measure

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Rezaei 2023 [103]	Supratentorial/infratentorial	All patients completed the study protocol, and no adverse effect was reported	Yes	No one
Sasaki 2017 [86]	The region of MCA	No patient experienced any pathological symptoms or deterioration of neurological symptoms	No	All patients completed the study protocol
Sasaki 2013 [87]	The region of MCA	No patient experienced any pathologic symptoms such as seizure or any deterioration of motor function in the affected upper limb during the study period	Yes	The protocol of this study was completed by all patients
Sengul 2023 [88]	Subcortical and cortical plus subcortical	No adverse events were observed during the intervention. In addition, no adverse events were reported to the investigators by the participants during the 3-month period after the intervention	Yes	None of the subjects dropped out of the study or analyses
Seniow 2012 [98]	Cortical and corticosubcortical	DR	No	Four patients from the E group and 2 from the C group were lost to follow-up
Sharma 2020 [64]	Large artery Lacunar Cardioembolic Others	One participant had seizure who was managed symptomatically	Yes	During the run-in period, 35 participants withdrew consent and 4 died after discharge from hospital. Seven participants in real rTMS were lost to follow-up
Shim 2023 [38]	Subcortex damage	DR	No	2 patients were excluded due to discharge, and 1 dropped out of the intervention
Shu 2024 [93]	DR	DR	No	Six of each group withdrew midway, with 30 for each group ultimately being included in statistical analysis
Takeuchi 2005 [65]	Subcortical infarction	Subjects did not report any adverse side effects during the course of the study	No	No one
Takeuchi 2008 [66]	Subcortical infarction	The subjects did not report any adverse effects during the course of the study	No	No one
Tosun 2017 [67]	DR	No adverse events were reported by any of the participants, all participants completed the trial	All patients completed trail	No one
Wang 2014 [89]	The region of MCA	All of the patients completed the experimental protocols and assessments and exhibited no notable adverse effects	No	All of the patients completed the experimental protocols

Table 3 (continued)

ID	The area of stroke	Intervention-related adverse events	Intent-to-treat analysis	Drop off
Wang 2022 [90]	Cortical Subcortical Brain stem	There were no severe adverse reactions such as seizures or recurrent stroke happened during all treatments. Only one patient in the HF-rTMS group experienced dizziness at the first few sessions of stimulation. No special treatment was performed, the symptom disappeared soon after intervention	Yes	All participants completed the trial
Wang 2024 [94]	DR	without any observed adverse events during treatment	Yes	No one
Wang 2020 [91]	The region of MCA	DR	Yes	All the patients completed treatments
Wang C 2023 [68]	Cortical Subcortical Both	DR	Yes	All patients completed study
Wang T 2023 [99]		DR	No	All patients completed study
Wu 2023 [100]	DR	No patient experienced any adverse reactions, such as epilepsy, pain, or deterioration of the condition	Yes	No one
Yang 2021 [101]	Cortex; Subcortex; Both	Finally, thirty-nine patients completed the interventions without incident, severe side effects, or discomfort, indicating that the procedure was well tolerated	No	Five patients dropped out of the trial due to personal problems
Yu 2022 [102]	Basal ganglia	DR	Yes	No one
Xie 2023 [95]	Supratentorial/infratentorial	DR	No	3 of the 10 dropouts were passive withdrawal due to hardware equipment problems, and 5 of the remaining 7 active withdrawal were from the sham group

MCA middle cerebral artery, *DR* do not report

and independent secretary [76]. Therefore, these studies were assessed as having a "low" risk of bias in the domain of "Allocation concealment (selection bias)". Conversely, other studies were identified as having unclear risks in this area. Thirty-two studies reported the blinding of participants [36, 39, 42–44, 47, 49, 50, 55–57, 59, 63, 64, 69, 70, 73–76, 78, 79, 82, 85–88, 92, 95, 98], indicating a low risk of bias in the domain of "Blinding of participants (performance bias)". Furthermore, five trials implemented rTMS operator blindness [39, 57, 73, 80, 90], demonstrating a low risk of bias in the category of "Blinding of rTMS intervention operators (performance bias)". Additionally, twenty-two studies implemented the blinding of rehabilitation therapists [36, 42, 43, 47, 49, 57, 64, 69–71, 75–79, 82–84, 86, 89, 92, 98], demonstrating a low risk of bias in the area of "Blinding of rehabilitation therapists (performance bias)". However, eight studies focused solely on comparing the efficacy difference between rTMS and sham interventions, without conducting any rehabilitation intervention [41, 48, 58, 72, 80, 85, 88, 95]. Consequently, these studies were categorized as not applicable in terms of "blinding of rehabilitation therapists", resulting in a blank box in the risk of bias summary. A total of forty-four studies provided explicit documentation of the blinding of the outcome assessmenter [28, 35, 36, 39, 40, 42–44, 47–50, 53–58, 62–64, 67, 69–71, 74–79, 81–83, 86–88, 90, 92, 95–98, 102], indicating a low risk of bias in the category of "Blinding of outcome assessment (detection bias)". In contrast, only nineteen studies reported the blinding of the data analyst [36, 40, 43, 47, 59, 63, 65–67, 70, 75, 76, 79, 81, 88, 90, 97, 98, 100], demonstrating a low risk of bias in the item of "Blinding of data analysts (detection bias)" category. Regarding incomplete outcome data, one trial reported that thirteen participants were excluded from the analysis, primarily because of incomplete data sets [35], which presents a high risk of bias in the "Incomplete outcome data (attrition bias)" category. Furthermore, nineteen studies were considered as having a high risk for other biases, due to factors such as small sample size, poor randomization and lack of blinding [38, 40–42, 45, 46, 48, 59, 60, 62, 68, 71, 72, 76, 78, 80, 86, 98, 99].

Effects of intervention

Motor function of the upper limb

Twenty-two studies, involving a total of 950 stroke patients, examined the effects of 1 Hz rTMS over the contralesional M1 on the motor function of the upper limb in stroke survivors measured using FMA-UL. The findings of these studies revealed that 1 Hz rTMS over the contralesional M1 was associated with improvements in motor function among stroke patients in the early stage (< 1 month) with a moderate effect size (study number: 10, $n = 443$, SMD = 0.44, 95% CI 0.24 to 0.63, $P < 0.00001$, $I^2 = 47\%$, fixed-effect model) as well as the recovery phase (1–6 months) with a moderate effect size (study number: 8, $n = 233$, SMD = 0.61, 95% CI 0.34 to 0.87, $P < 0.00001$, $I^2 = 33\%$, fixed-effect model). However, the available evidence does not support the notion that 1 Hz rTMS can enhance motor function in individuals with chronic stroke (> 6 months) with a small effect size (study number: 4, $n = 274$, SMD = 0.13, 95% CI − 0.11 to 0.36, $P = 0.28$, $I^2 = 0\%$, the fixed-effect model) by increasing FMA-UL scores (as shown in Fig. 3A and the SI Table S2). Moreover, six trials investigated the effects of 10 Hz rTMS on stroke patients. The overall results showed that 10 Hz rTMS over the ipsilesional M1 can improve the motor function of upper limbers among stroke patients in the early stage (< 1 month) with a large effect size (study number: 3, $n = 229$, SMD = 0.75, 95% CI 0.49 to 1.02, $P < 0.\ 00001$, $I^2 = 0\%$, fixed-effect model, Fig. 3B and SI Table S2) using the FMA-UL score. The included studies employed various assessment tools to evaluate upper limb motor function, such as the grip strength of limb, JTHFT, the Nine-Hole Peg Test (NHPT), the Purdue Pegboard test (PPT), WMFT, BBT, and the Action Research Arm Test (ARAT).

Motor function of the lower limb

Eight trials were conducted to investigate the impact of 1 Hz rTMS over the contralesional M1 on the motor function of the lower limb in stroke survivors, as measured by FMA-LL. The findings of these trials revealed that 1 Hz rTMS has the potential to increase the FMA-LL score in both early-stage stroke patients (< 1 month) with a moderate effect size ($n = 166$, SMD = 0.67, 95% CI 0.35 to 0.99, $P < 0.0001$, $I^2 = 60\%$, fixed-effect model, Fig. 3C and SI Table S2) and recovery phase patients (1–6 months) with a moderate effect size ($n = 223$, SMD = 0.59, 95% CI 0.32 to 0.86, $P < 0.0001$, $I^2 = 0\%$, fixed-effect model, Fig. 3C and SI Table S2). The included studies employed additional measures to evaluate lower limb motor function, including the10MWT, the 6MWT and the Brunnstrom-Low test, with small samples.

Motor function using MAS/AS

MAS/AS was used to assess motor function in six studies. The results did not support that 1 Hz rTMS over the contralesional M1 could improve the MAS score for stroke less than 1 month with a small effect size ($n = 58$, SMD = 0.03, 95% CI − 0.49 to 0.54, $P = 0.39$, $I^2 = 0\%$, the fixed-effect model, SI Table S2), for the stroke with a small effect size (1–6 months) ($n = 107$, SMD = − 0.15,

95% CI − 0.54 to 0.23, $P = 0.25$, $I^2 = 28\%$, the fixed-effect model, SI Table S2), and for stroke more than 6 months with a moderate effect size ($n = 21$, SMD = − 0.49, 95% CI − 1.36 to 0.39, $P = 0.27$, the fixed-effect model, SI Table S2).

Activities of daily living (ADLs)

Fifteen studies were conducted to investigate the effects of 1 Hz rTMS over the contralesional M1 on ADLs in individuals with stroke using the MBI or BI. The results indicated that 1 Hz rTMS over the contralesional M1 was found to significantly improve ADLs in individuals with stroke within 1 month of onset with a moderate effect size ($n = 343$, SMD = 0.67, 95% CI 0.44 to 0.89, $I^2 = 79\%$, $P < 0.00001$, fixed-effect model, Fig. 4A and SI Table S2). However, no significant improvement in ADL was observed for individuals with stroke beyond 1 month (Fig. 4A and SI Table S2). Additionally, five studies examined the effect of 10 Hz rTMS on stroke and the results demonstrated that 10 Hz rTMS over the ipsilesional M1 can improve ADLs in individuals with stroke within 1 month of stroke onset with a large effect size ($n = 160$, SMD = 1.98, 95% CI 1.60 to 2.36, $P < 0.00001$, fixed-effect model, Fig. 4B and SI Table S2) and with the relatively small sample size. However, evidence suggesting that 3 Hz or 5 Hz rTMS can improve the ADLs for stroke patients between the 1–6 months is a lacking (SI Table S2).

Neurological function

There is no evidence to suggest that 1 Hz rTMS over contralesional M1 can improve the NHISS score for the stroke-related neurological impairment with a small effect ($P = 0.18$, $P = 0.61$ and $P = 0.73$, respectively, as shown in Fig. 5A and SI Table S2). However, four studies examining the effects of 3 Hz rTMS on stroke patients within 1 month of onset indicated that 3 Hz can improve the NHISS score with a large effect ($n = 154$, SMD = − 0.73, 95% CI − 1.06 to − 0.41, $I^2 = 0\%$, $P < 0.0001$, fixed-effect model, as shown in Fig. 5B and SI Table S2).

Using RMT of unaffected hemisphere, 1 Hz rTMS over the contralesional M1 has a supportive effect on the recovery of unaffected hemispheres in stroke patients within 1 month of onset with a moderate effect ($n = 123$, SMD = 0.67, 95% CI 0.30 to1.03, $I^2 = 0\%$, $P = 0.0003$, fixed-effect model, Fig. 6A and SI Table S1). The results suggest that 1 Hz rTMS over the contralesional M1 can improve the amplitude of contralesional motor evoked potentials (MEPs) in individuals with stroke within 1 month of onset with a moderate effect ($n = 167$, SMD = − 0.58, 95% CI − 0.90 to − 0.27, $I^2 = 0\%$, $P = 0.0003$, fixed-effect model, Fig. 6B and SI Table S2). Furthermore, the study revealed that 1 Hz rTMS improve the amplitude of ipsilesional MEPs in individuals with stroke within 1 month of onset with a large effect ($n = 121$, SMD = 1.09, 95% CI 0.70 to 1.48, $I^2 = 50\%$, $P < 0.0001$, fixed-effect model, Fig. 6C and SI Table S2).

Drop out

Information for the drop-offs in each study is shown in Table 3. A total of twenty-seven studies carried out intent-to-treat analyze [28, 39, 44, 48, 51, 52, 54–57, 64, 67, 74–76, 83, 84, 86, 87, 90–92, 94, 99, 100, 102, 103]. Eight studies did not report information of on drop-off [45–47, 65, 66, 69, 71, 85]. Twenty-seven studies reported that all patients completed protocols [39–41, 51, 52, 55, 58, 60, 67, 78, 81, 82, 84–86, 88–90, 92, 94, 98, 99, 102, 103].

Adverse events

Twenty-two studies did not report information on adverse events [39–41, 45, 46, 50–52, 61–63, 69, 71, 72, 78, 81, 83, 95, 98, 99, 102, 104], whereas twenty-three studies reported that no patients experienced any adverse reactions [49, 54, 56–58, 65–67, 70, 74, 76, 81–83, 85–89, 94, 100, 101, 103]. However, 21 studies reported various adverse events, such as epileptic seizures, headaches, anxiety, tiredness, pain, spasm, myalgia, paresthesia, and drowsiness [28, 35–37, 42–44, 47, 48, 53, 59, 60, 64, 73, 75, 77–80, 90, 96].

Sensitivity analysis

The detailed analysis process and the treatment taken are shown in the SI Table S1. The random-effects model was employed instead of the fixed-effects model for subgroups exhibiting substantial heterogeneity across studies. The robustness of the findings was evaluated via a sensitivity analysis, in which each included study was systematically excluded, and the effect sizes were recalculated to detect any variations. This approach also enables the identification of studies that exert significant influence on the overall results and assists in examining clinical heterogeneity. The analysis demonstrated that the effect sizes remained largely consistent upon the exclusion of individual studies, thereby indicating the stability of the study's findings (Fig. 7A–D and SI Table S3 to Table S6).

Publication bias

Despite the Cochrane Handbook's recommendation to apply publication bias for outcomes reported in more than 10 studies, Egger's test was still conducted for 1 Hz rTMS on MBI/BI due to the inclusion of more than 5 studies and a total participant count exceeding 250. The findings suggest that there is no evidence of publication

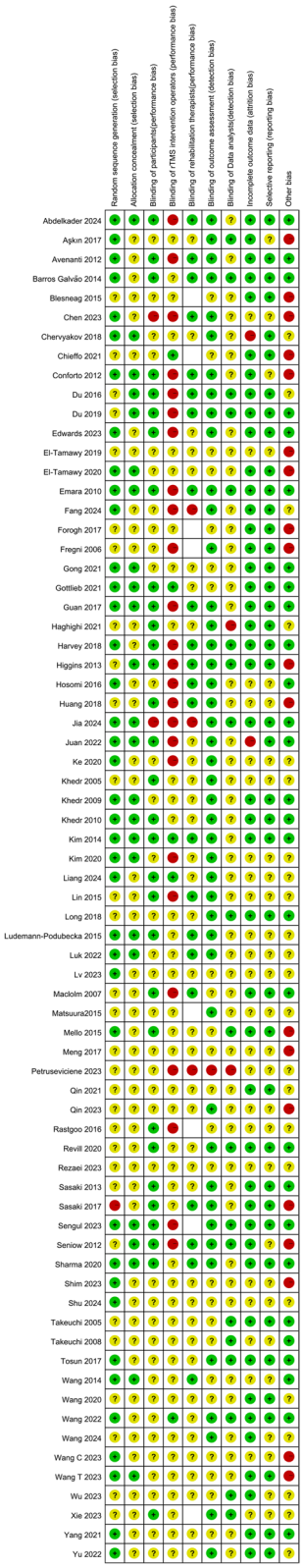

Fig. 2 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

bias in relation to the FMA-UL at a frequency of 1 Hz for stroke patients within the first month of onset ($P=0.94$), as well as for stroke patients between 1 and 6 months post onset ($P=0.831$). Similarly, the same lack of publication bias was observed for the MBI at a frequency of 1 Hz for stroke patients within the first month of onset ($P=0.508$), and for stroke patients between 1 to 6 months post onset ($P=0.418$).

The quality of evidence

The level of evidence supporting the use of 1 Hz rTMS over the contralesional M1 for stroke (within 1 month) using FMA-UL and MBI was increased as a result of a substantial sample size exceeding 300 participants. However, for other outcomes, the level of evidence was decreased due to imprecision resulting from a small sample size and publication bias. Consequently, the level of evidence was downgraded. Finally, the quality of evidence for the effect of 1 Hz rTMS over the contralesional M1 on motor function (FMA-UL) in stroke patients within 1 month was determined to be "high quality". The quality of evidence for other outcomes, such as 1 Hz rTMS over the contralesional M1 for stroke between 1 and 6 months on FMA-UL and 1H z rTMS over the contralesional M1 for stroke patients within 1 month on MBI/BI, were downgraded to "moderate quality", whereas for other outcomes, not mentioned above, the quality of evidence were also downgraded to "low" or "very low quality" (Table 4).

Discussion

This research adhered to the rigorous methodological guidelines outlined in the Cochrane intervention Handbook. As reported in the previous literature [105], the scope of this study was limited to English literature but considers all health-related areas. The databases were selected cross-disciplinary research, which can provide a wide range of opinions. The process of study selection comprises a systematic search of literature sources followed by three iterative stages of screening and filtering. In the initial stage, duplicate articles are excluded, and relevant articles are collected using Endnote software. The second stage involves screening titles and abstracts to exclude articles that fall outside the scope of the research domain. Finally, the third stage entails a thorough full-text review to exclude articles that do not meet the specified domain and criteria. And additional records identified through reference of full text. All iterations adhere to consistent eligibility criteria and are subsequently subjected to a process of screening and review. During the data extraction process, the initial data were independently extracted by one researcher and subsequently verified by another. For the studies that did

report the raw data, data extraction software (Getdata 2.2) was used to obtain relevant information from statistical charts by two well trained authors. Any missing data were acquired through communication with the original author via email. The above process ensures the completeness, accuracy and reliability of the data, which are core elements of high-quality data. In the context of healthcare decision-making, the availability of accurate and reliable predictions is of paramount importance, underscoring the crucial role of data quality [106]. For this reason, our findings can aid healthcare practitioners in making educated decisions.

Prior to commencing the study, a well-structured study protocol was developed, reviewed by experts, and made available online, thereby ensuring the reliability and validity of the findings. The process of literature screening, data extraction, and data analysis was independently conducted by two authors, with a consensus reached through the involvement of a third author to ensure internal consistency. Following the completion of data analysis, the literature was updated until July 29, 2024, to ensure the timeliness of the results. This review specifically included studies that focused on the use of simple rTMS either alone or in combination with rehabilitation, excluding studies involving complex-pattern rTMS. This approach aimed to establish a clear association between rTMS and its impact on motor function and ADLs. The subgroup analysis of different frequencies of rTMS and durations of stroke explained the clinical heterogeneity and methodological heterogeneity.

The study included a total of seventy RCTs that involved 2951 patients across various stages of stroke, including early-stage stroke, recovery-phase stroke, and chronic stroke. The existing evidence indicates that the efficacy of different frequencies of rTMS in ameliorating motor dysfunction among stroke patients varies inconsistently across different stages. The results derived from the FMA-UL suggest that rTMS at frequencies of 1, 10, and 20 Hz may exert a beneficial effect on upper limb motor function in patients with early-stage stroke (< 1 month). Specifically, the SMD analysis suggests that 1 Hz rTMS has a moderate effect on enhancing upper limb motor function, whereas 10 and 20 Hz rTMS demonstrate a large effect size. Nonetheless, these conclusions should be interpreted with caution in clinical practice due to limitations such as the small sample size, the low quality of the included studies, and other confounding factors. The moderate effect size observed for 1 Hz rTMS over the contralesional M1 suggests its potential to positively influence upper limb motor function recovery during the stroke recovery phase. However, the results of grip strength assessments did not indicate that 1 Hz over the contralesional M1 or 10 Hz rTMS over ipsilesional M1 provides positive benefits for individuals in the early stages of stroke. In terms of ADLs, the overall results suggest that 1 Hz over the contralesional M1, 3 Hz over the ipsilesional M1, 10 Hz over the ipsilesional M1, and 20 Hz over the ipsilesional M1 rTMS may offer potential benefits for early-stage stroke patients. Specifically, the SMD result suggests that 1 Hz stimulation over the contralesional M1 exerts a moderate effect on improving upper limb ADLs, whereas 10 and 20 Hz rTMS over the ipsilesional M1 exhibit a large effect size. However, these findings should be approached with caution in clinical practice due to limitations such as small sample sizes, the low quality of the included studies, and other confounding variables. However, the current evidence does not support the notion that rTMS can improve neurological function scores as measured by the NHISS. The primary outcomes, namely FMA-UL, FMA-LL, grip strength, and MAS/AS, exhibited varying levels of evidence. Specifically, the evidence supporting the efficacy of 1 Hz rTMS over the contralesional M1 for early-stage stroke motor function was upgraded to a "high-quality" rating. Conversely, the evidence pertaining to other outcomes was downgraded to "moderate-quality", "low-quality", and "very low-quality" ratings. This decision was influenced by the presence of substantial clinical heterogeneity and limited sample sizes.

Despite successfully demonstrating the benefits of rTMS for stroke patients, this study has notable limitations that warrant attention. Importantly, significant clinical heterogeneity was observed across studies, which stemmed from variations in disease periods, injury sites, intervention timing, intervention type, frequency, control measures, site of application, duration, and assessment instruments. The second concern pertains to the inclusion of patients in certain studies who were unaware of rTMS and were exposed to simulated sounds or counterfeit coils, albeit not in an entirely identical manner. While the sensation experienced on the scalp may be similar similarities, it cannot be considered identical to that of the rTMS group. The third point of consideration pertains to the challenging nature of implementing rTMS operator blinding, thereby categorizing operator blindness as a high-risk factor. Furthermore, the fourth aspect to contemplate involves the limited sample size, absence of intention-to-treat analysis reporting, and methodological deficiencies, all of which contributed to a reduction in the quality of our evidence. The final and paramount inquiry that warrants our attention pertains to the limited ability to ascertain the safety of implementing rTMS due to inadequate and inconsistent documentation of adverse events, such as epileptic seizures, headaches, anxiety, fatigue, pain, spasms, myalgia, paresthesia, and drowsiness, which have only been partially reported in

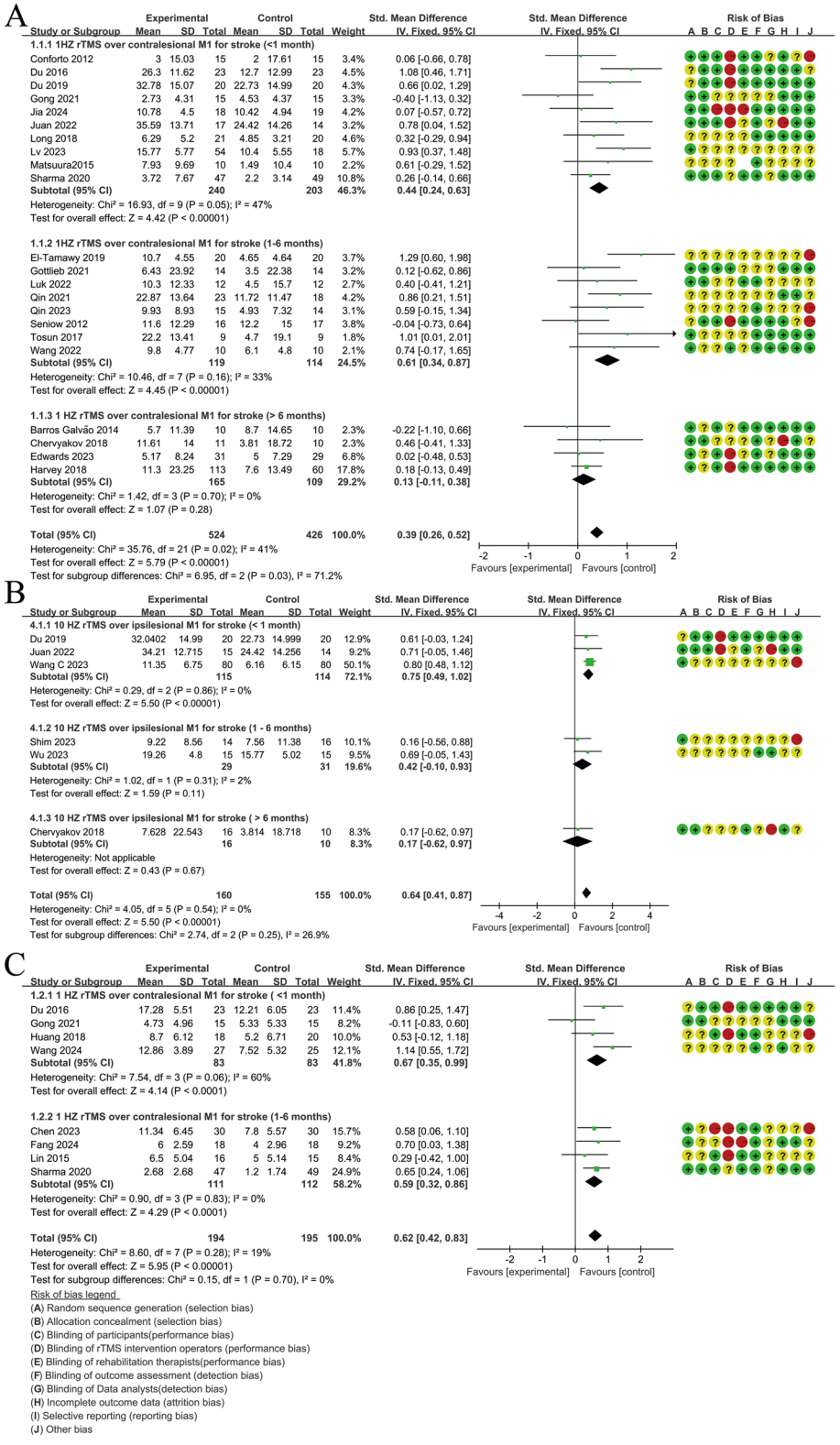

Fig. 3 **A** Meta-analysis of 1 Hz rTMS over contralesional M1 for stroke on FMA-UL. **B** Meta-analysis of 10 Hz rTMS over ipsilesional M1 for stroke on FMA-UL. **C** Meta-analysis of 1 Hz rTMS over contralesional M1 for stroke on FMA-LL

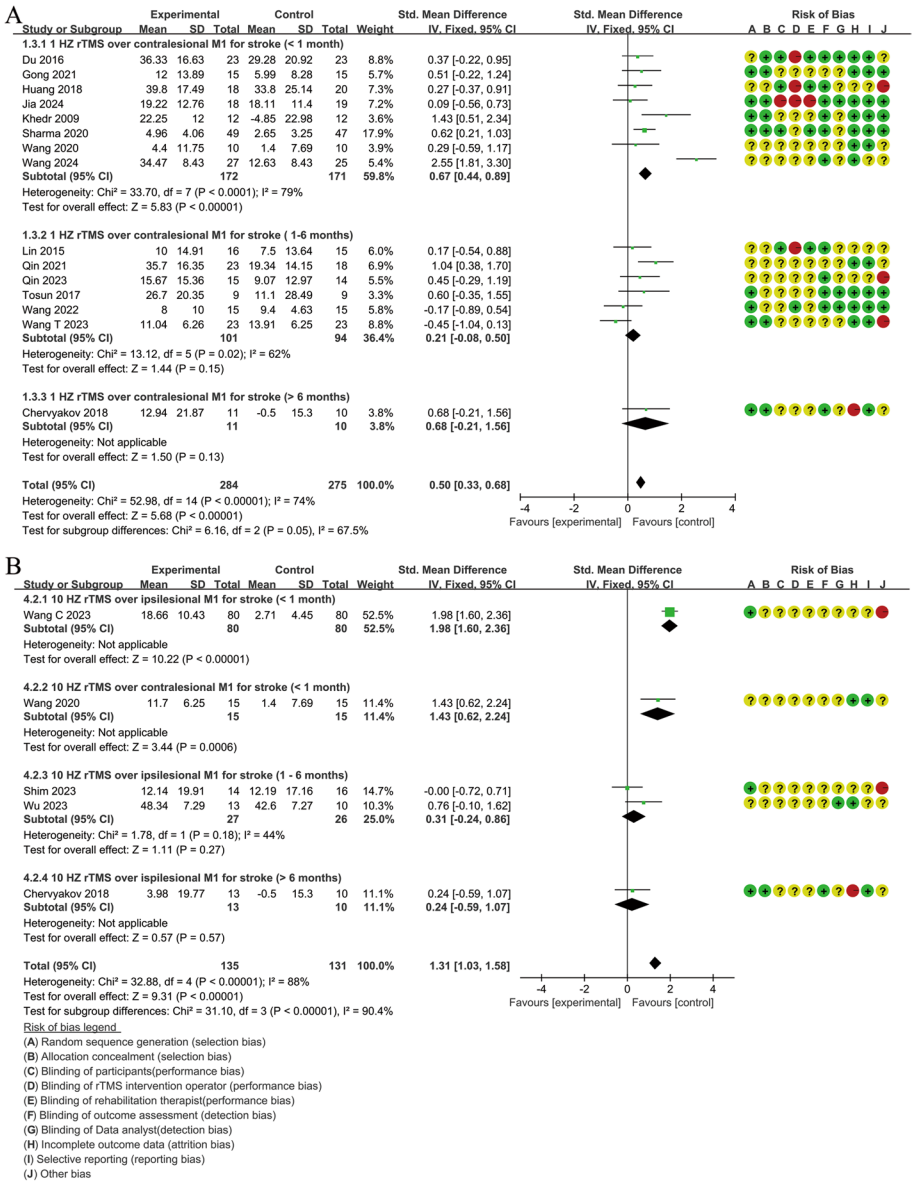

Fig. 4 **A** Meta-analysis of 1 Hz rTMS over contralesional M1 for stroke on MBI. **B** Meta-analysis of 10 Hz rTMS (contralesional M1 or ipsilesional M1) for stroke on MBI

certain studies. Consequently, it is imperative to exercise caution when evaluating the robustness of the evidence.

Future research directions

This study significantly contributes to our comprehension of the impact of rTMS on the motor function of stroke patients. Furthermore, it offers valuable insights and recommendations for future investigations. The recovery of motor function in stroke patients is intricately linked to the specific location and type of stroke. However, the present studies encompassed the utilization of comparable interventions in stroke patients with diverse site injuries (cortical, subcortical, or others) and distinct types (ischemic and hemorrhagic stroke). Importantly, the baseline motor function following a stroke serves as a significant indicator of eventual functional recovery post-stroke. The initial motor function status of stroke patients should be taken into account during the assessment of treatment effectiveness. For example, ensuring that groups are matched for initial motor function impairment can enhance the assessment of the effectiveness of rTMS.

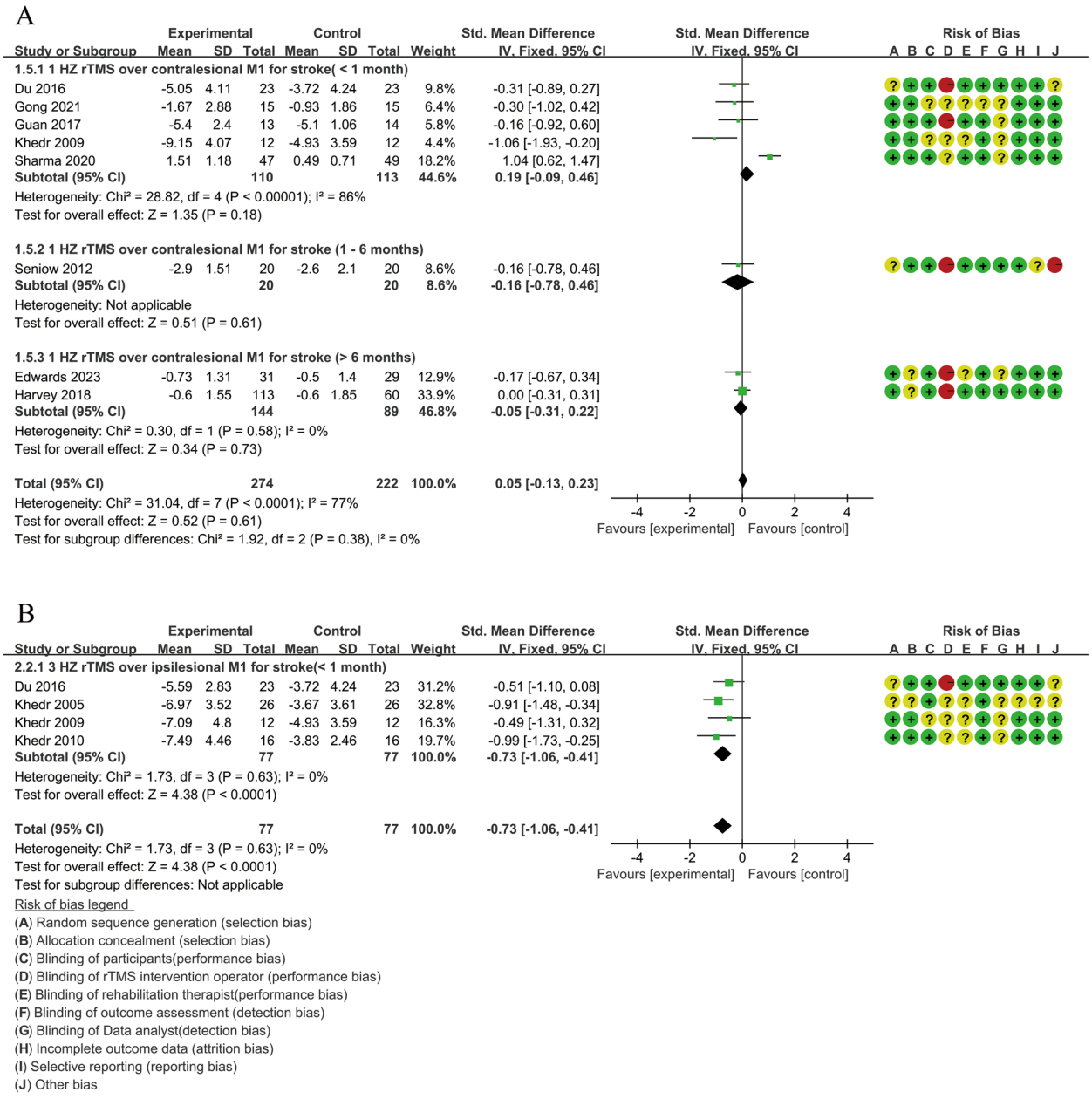

Fig. 5 **A** Meta-analysis of 1 Hz rTMS over contralesional M1 for stroke on NHISS. **B** Meta-analysis of 3 Hz rTMS over ipsilesional M1 for stroke on NHISS

Hence, patient stratification becomes imperative when formulating treatment plans for future studies. Trials evaluating rTMS focused on the motor domain should carefully consider selecting endpoint measures that are tailored to assess motor impairment, capacity, and performance. In early-phase exploratory trials, the use of measures at all three levels could provide valuable insights, whereas later-phase trials may benefit from prioritizing measures of capacity and performance that effectively capture the impact of the intervention on patients' daily activities and participation. Broad measures of independence or disability, such as the modified Rankin scale, may lack the necessary sensitivity to serve as primary endpoint measures. Therefore, carefully selecting domain-specific endpoint measures that align with the intervention objectives, the patient's stage of stroke recovery, and the stroke phase is crucial. Moreover, previous studies on rTMS have focused

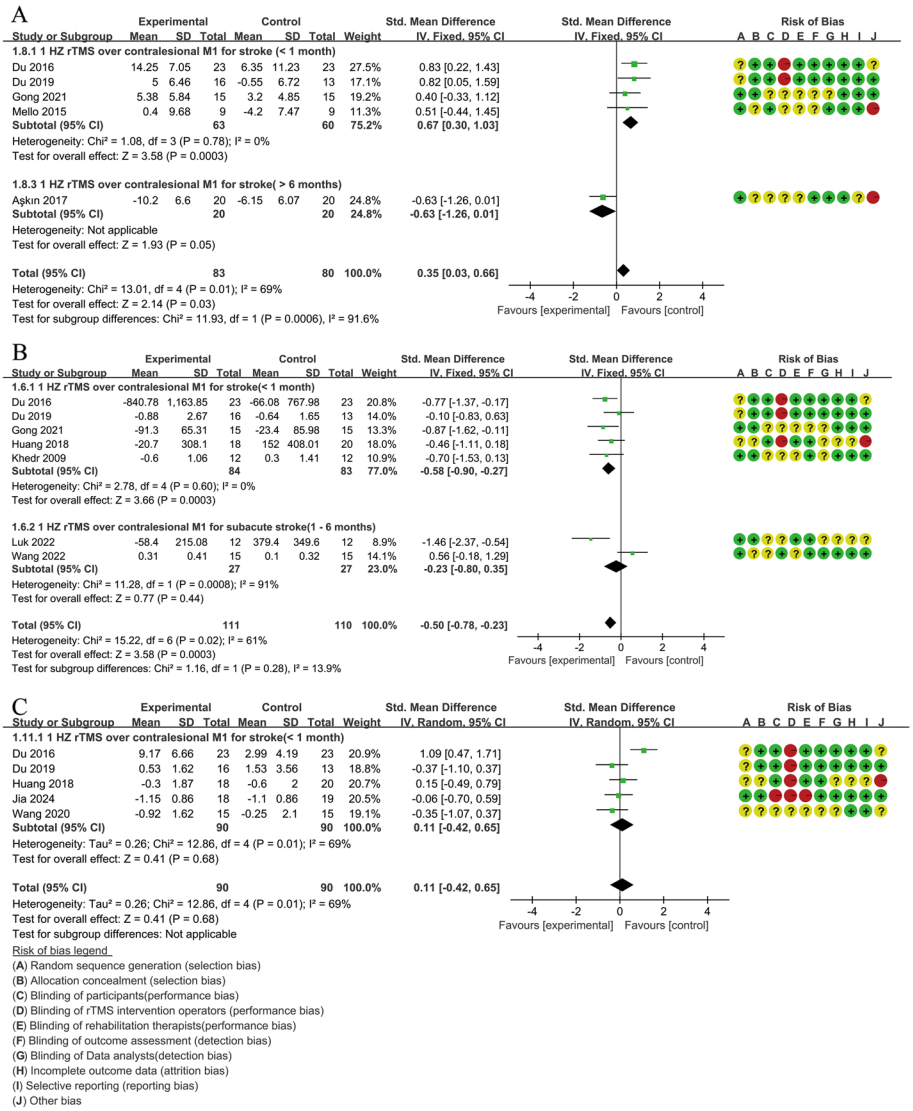

Fig. 6 **A** Meta-analysis of 1 Hz rTMS over contralesional M1 for stroke on rMT of unaffected hemisphere. **B** Meta-analysis of 1 Hz over contralesional M1 for stroke on amplitude of contralesional MEPs. (C) Meta-analysis of 1 Hz over contralesional M1 for stroke of Latency of contralesional MEPs

primarily on factors such as suitability, patient comfort, availability of stimulation devices, and impact on corticospinal excitability, without considering the underlying mechanism of action. Therefore, an optimal rTMS regimen should be contingent upon the patient's functional preservation, the specific type of stroke (subcortical or cortical; ischemic or hemorrhagic), and the stage of stroke (early stage, convalescence, or chronic period). The use of rTMS exhibits considerable inter-individual variability. This variability is often attributed to the stimulation parameters employed to enhance corticospinal excitability, because the protocol's impact on a diverse population of cortical neurons can result in an inhibitory effect. The clinical heterogeneity observed in rTMS trials for stroke primarily stems from variations in stimulus programs, such as the number of sessions administered and the duration of concurrent physical therapy. These variations have constrained the outcomes of rTMS trials for stroke. Intervention parameters, such as location of the coil, intensity, cycle treatment, and stroke type, increased the variability of the study. Few studies have examined the relationships between stimulation parameters and neurophysiological assessments of the motor system, as well as the impact of the interventions on excitation connectivity and clinical outcomes. Consequently, the selection of rTMS intervention parameters should be guided by test findings, such as functional magnetic resonance

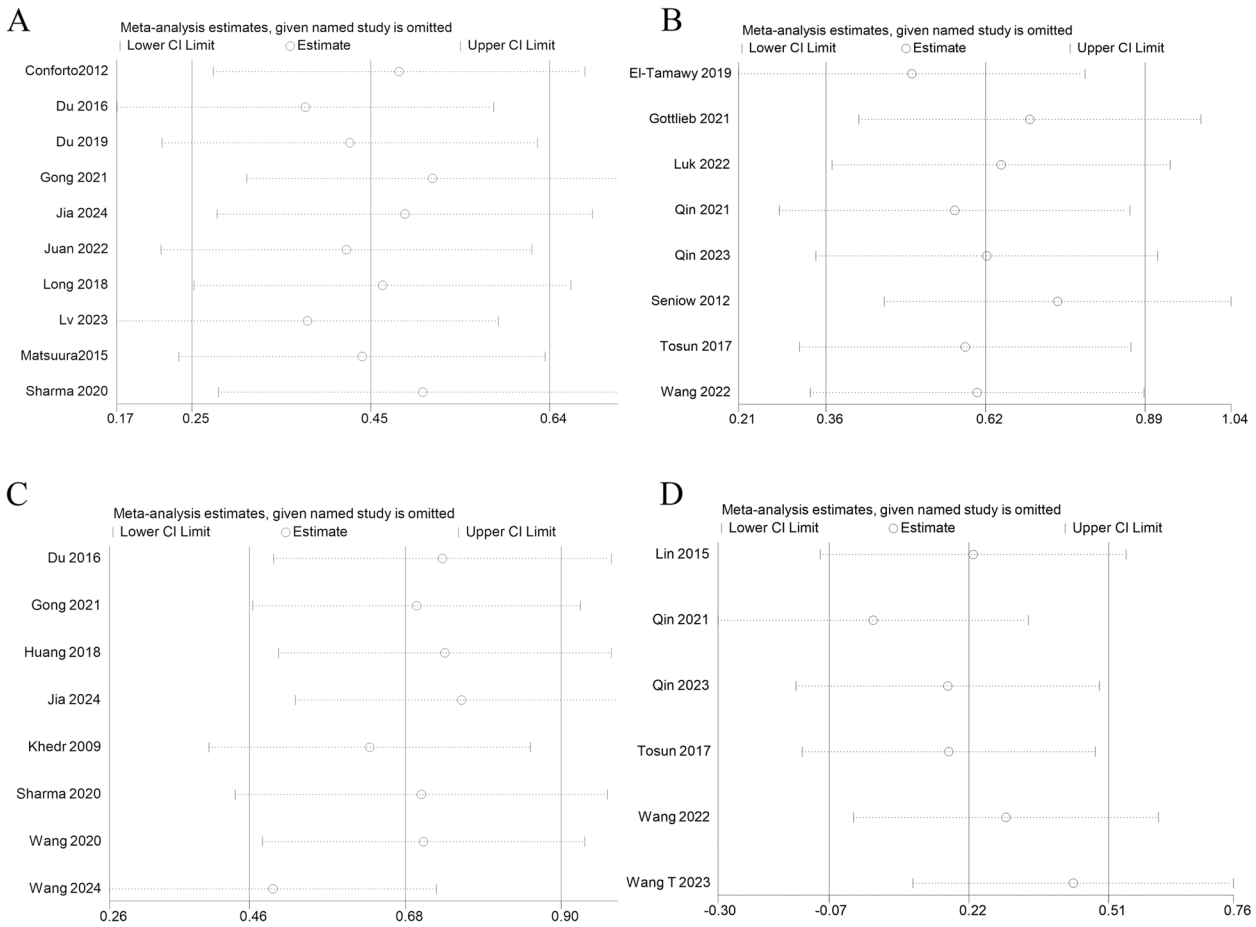

Fig. 7 **A** Sensitivity analysis of 1 Hz rTMS over contralesional M1 for stroke (< 1 month) on FMA-UL. **B** Sensitivity analysis of 1 Hz rTMS over contralesional M1 for stroke (1–6 months) on FMA-UL. **C** Sensitivity analysis of 1 Hz rTMS contralesional M1 for stroke (< 1 month) on MBI/BI. **D** Sensitivity analysis of 1 Hz rTMS contralesional M1 for stroke (1–6 months) on MBI/BI

imaging (fMRI), magnetic resonance spectroscopy, near infrared spectroscopy (NIR), EEG, and other detection methods. These tools provide a comprehensive understanding of the specific mode of operation employed by patients and the natural activities occurring during rTMS intervention. This understanding is crucial for the successful implementation of personalized rTMS programs. Additionally, the preceding study failed to establish a definitive correlation between the efficacy of rTMS and the degree of stimulation, thereby highlighting the significance of investigating this crucial aspect in subsequent research endeavors. Notably, during the acute phase, MEPs are frequently not elicited on the affected side even when the stimulation intensity is at its maximum [15]. In patients who retain MEPs, it was observed that the threshold for movement on the affected side is typically elevated, whereas the threshold for MEPs is reduced compared with that on to the unaffected or healthy side [107, 108]. Within the initial months, MEPs may resurface and progressively amplify, whereas the motion threshold tends to diminish [104, 109]. Numerous scholars have proposed that the evaluation of early corticospinal tract integrity and the enhancement of corticospinal tract integrity through rTMS during the early recovery phase are linked to enduring functional outcomes [110]. Hence, acknowledging the potential influence of the integrity of the spinal cord cortex on the effectiveness of TMS is imperative and warrants further investigation in subsequent research endeavors. Moreover, the issue of

Table 4 The level of GRADE for outcomes

Outcomes/subgroup	Comments	No of participants (studies)	Quality of the evidence(GRADE)
FMA-UL			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD 0.44 (0.24 to 0.63)	443 (10 studies)	⊕⊕⊕⊕ **high**[1,3]
1 Hz rTMS over contralesional M1 for stroke (1–6 months)	SMD 0.61 (0.34 to 0.87)	233 (8 studies)	⊕⊕⊕⊖ **moderate**[2,3]
1 Hz rTMS over contralesional M1 for stroke (> 6 months)	SMD 0.13 (− 0.11 to 0.38)	274 (4 studies)	⊕⊕⊖⊖ **low**[1,2]
10 Hz rTMS over ipsilesional M1 for stroke (< 1 month)	SMD 0.75 (0.49 to 1.02)	229 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
10 Hz rTMS over ipsilesional M1 for stroke (1–6 months)	SMD 0.42 (− 0.10 to 0.93)	60 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
Grip strength of affected limb			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD 0.37 (− 0.15 to 0.88)	62 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
1 Hz rTMS over contralesional M1 for stroke (1–6 months)	SMD 0.32 (− 0.27 to 0.92)	44 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
FMA-LL			
1 HZ rTMS over contralesional M1 for stroke (< 1 months)	SMD 0.67 (0.35 to 0.99)	166 (4 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
1 HZ rTMS over contralesional M1 for stroke (1–6 months)	SMD 0.59 (0.32 to 0.86)	223 (4 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
MBI/BI			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD 0.67 (0.44 to 0.89)	343 (8 studies)	⊕⊕⊕⊖ **moderate**[1,2,3]
1 Hz rTMS over contralesional M1 for stroke (1–6 months)	SMD 0.21 (− 0.08 to 0.50)	195 (6 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
MAS/AS			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD 0.03 (− 0.49 to 0.54)	58 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
1 Hz rTMS over contralesional M1 for stroke (1–6 months)	SMD − 0.15 (− 0.54 to 0.23)	107 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
1 Hz rTMS over contralesional M1 for stroke (> 6 months)	SMD − 0.49(− 1.36 to 0.39)	21 (1 study)	⊕⊖⊖⊖ **very low**[1,2,4]
NHISS			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD − 0.19 (− 0.09 to 0.46)	223 (5 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
1 Hz rTMS over contralesional M1 for stroke (> 6 months)	SMD − 0.05 (− 0.31 to 0.22)	233 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
3 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD − 0.73 (− 1.06 to − 0.41)	154 (4 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
Amplitude of ipsilesional of MEPs			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD 1.09 (0.70 to 1.48)	121 (4 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
Amplitude of Contralesional MEPs			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD − 0.58 (− 0.90 to − 0.27)	167 (5 studies)	⊕⊖⊖⊖ **very low**[1,2]
1 Hz rTMS over contralesional M1 for stroke (1–6 months)	SMD − 0.23 (− 0.80 to − 0.35)	54 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
rMT of affected hemisphere			
1 Hz rTMS over contralesional M1 for stroke (< 1 month)	SMD − 0.48 (− 0.87 to − 0.09)	105 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,4]
BBT affected hand			
1 Hz rTMS over contralesional M1 for stroke (1–6 months)	SMD 0.00 (− 0.59 to 0.59)	44 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]

Table 4 (continued)

Outcomes/subgroup	Comments	No of participants (studies)	Quality of the evidence(GRADE)
1 Hz rTMS over contralesional M1 for stroke (> 6 months)	SMD 0.03 (− 0.54 to 0.60)	48 (2 studies)	⊕⊖⊖⊖ **very low**[1,2,4]

[*] The basis for the assumed risk (e.g., the median control group risk across studies) is provided in footnotes

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: We are very uncertain about the estimate

[1] High risk of bias, Downgrade quality of evidence (− 1)

[2] Less than 10 studies, Downgrade quality of evidence (− 1)

[3] More than 300 patients, Upgrade quality of evidence (+ 1)

[4] Small sample size, Downgrade quality of evidence (− 1)

spatial and temporal sensitivity has long been a prominent consideration in the realm of non-invasive interventions for stroke treatment. Precise spatial sensitivity cannot be quantified with absolute precision because of the variability in factors such as the number of coils in the device and the magnitude of the stimulus current, which determine the precise positioning and depth of the stimulus. Notably, circular and figure-8 coils yield distinct magnetic field ranges and stimulation points. Therefore, forthcoming studies should allocate greater consideration to this particular facet.

Conclusion

The application of rTMS in stroke patients, especially in improving the motor function of patients, brings hope to patients. However, the current research findings have introduced considerable ambiguity for health policymakers, clinicians, patients, and their families. This study adhered to a meticulously structured protocol, thereby ensuring the reliability and validity of the findings. After rigorous literature screening, data analysis, and evaluation of evidence quality, the results of this study showed that 1 Hz rTMS over the contralesional M1 may enhance motor function during the early stages of stroke and the recovery period and 1 Hz rTMS over the contralesional M1 can improve ADLs for stroke patients (1–6 months) of the event. Despite the inability to locate certain sources of "grey" literature, their inclusion is unlikely to have significantly impacted our results. It is crucial to interpret these findings with caution in clinical practice due to the small sample sizes and the low quality of the studies reviewed. The efficacy of 3, 5, 10, and 20 Hz rTMS in the treatment of motor dysfunction following stroke requires further investigation. To be specific, meticulously planned, multi-center, large-scale trials are needed to assess the safety and clinical efficacy of 3, 5, 10, and 20 Hz rTMS in individuals afflicted by stroke.

Abbreviations

rTMS	Repetitive transcranial magnetic stimulation
RCTs	Randomized controlled trials
FMA-UL	Fugl-Meyer Assessment Upper Limb subscale
FMA-LE	Fugl-Meyer Assessment Lower Limb subscale
MBI	Modified Barthel Index
BI	Barthel Index
NIBS	Non-invasive brain stimulation
IHI	Interhemispheric inhibition
LF-rTMS	Low-frequency rTMS
HF-rTMS	High-frequency TMS
θTBS	Theta burst stimulation
cTBS	Continuous TBS
iTBS	Intermittent TBS
PPS	Paired pulse stimulation
QPS	Quadripulse stimulation
PAS	Termed paired associative stimulation
M1	Primary motor cortex
ADLs	Activities of daily living
MEPs	Motor-evoked potentials
SI	Supplementary Information
MRC	the Medical Research Council Scale
FMA	Fugl-Meyer Assessment Scale
FAC	Functional ambulation classification
MRCP	Movement-related cortical potential
GCS	Glasgow Coma Scale
AMT	Active Motor Threshold
RMT	Resting motor threshold
MAS	Modified Ashworth Scale
BBT	Box and Block test
BRS	Brunnstrom Recovery Stages
ROM	Range of motion
10MT	Ten-meter walking test
6MWT	Six-min walking test
JHFT	Jebsen-Taylor Hand Function Test
BBS	Berg Balance Scale
ARAT	Action Research Arm Test
PASS	Postural Assessment Scale for Stroke
POMA-b	Balance subscale of the Tinetti Performance Oriented Mobility
WMFT	Wolf Motor Function Test
TUGT	Timed Up and Go Test
NHISS	National Institute of Health stroke scale
SIS	Stroke Impact Scale
SSQOL	Stroke Specific Quality of Life Scale
EQ-5D	EuroQoL Five Dimensions Questionnaire

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-025-02794-3.

Additional file 1.

Additional file 2.

Research registration unique identifying number

INPLASY, Registration number is INPLASY202360042. DOI number is https://doi.org/10.37766/inplasy2023.6.0042.

Authors' contributions

J.L.L. and K.Y. conceived and designed the study; G.L.X. and T. W. screened the records and wrote the paper; L. D., L.M.Z., and L.L. extracted data; C.Y.Z. and L.L. carried out quality evaluation of the included studies; H.M.S. and J.L.L. carried out evidence level determination. X.Z. and L.L. carried out data analysis. All authors contributed to draft the manuscript and have read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding

This study was supported by the National Natural Science Foundation of China (NSFC) (NO.82360969), Young Talents Project of Yunnan Province "Xingdian Talents Support Program" (XDYC-QNRC-2022–0269), Joint project of Department of Science and Technology of Yunnan Province-Yunnan University of Chinese Medicine (202101AZ070001-220), Traditional Chinese Medicine (TCM) high-level personnel training program of Yunnan Province (2024) and Yunnan province innovation team of prevention and treatment for brain diseases with acupuncture and Tuina (NO.202405AS350007). The funders were not involved in the study design; data collection, analysis, or interpretation; or writing the report. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and accuracy of the data analysis.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 18 March 2024 Accepted: 7 February 2025
Published online: 24 February 2025

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