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ORIGINAL RESEARCH

Transcutaneous Vagus Nerve Stimulation Combined with Rehabilitation Training in the Intervention of Upper Limb Movement Disorders After Stroke: A Systematic Review

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Introduction: Stroke often leaves behind a wide range of functional impairments, of which limb movement disorders are more common. Approximately 85% of patients have varying degrees of upper limb motor impairment. In recent years, transcutaneous vagus nerve stimulation combined with rehabilitation training has been gradually used in the rehabilitation of upper limb motor dysfunction after stroke and appears to have some therapeutic benefits.

Purpose: We conducted the systematic review to evaluate the efficacy and safety of transcutaneous vagus nerve stimulation combined with rehabilitation training in the rehabilitation of upper limb motor dysfunction after stroke.

Methods: Six databases, including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure Database (CNKI), Wanfang Database, and China Science and Technology Journal Database (VIP), were searched for January 1, 2016 to January 30, 2022. Randomized controlled trials using TVNS combined with rehabilitation training to intervene in upper limb motor dysfunction after stroke were included, and meta-analysis was performed using Review Manager 5.4.1 software.

Results: Total of 101 participants from 4 studies were included in this systematic review. These studies were evaluated using the Cochrane Review's Handbook 5.1 evaluation criteria and PEDro scores, and meta-analysis was performed on the collected data. The systematic review shows a significant effect of TVNS combined with rehabilitation training on the Upper Extremity Fugl-Meyer Score (MD=3.58, 95% CI [2.34, 4.82], P<0.00001, I2=0%), Function Independent Measure Score (MD=3.86, 95% CI [0.45, 7.27], P=0.03, I2=0%) and the Wolf Motor Function Test Score (MD=3.58, 95% CI [1.97, 5.18], P<0.0001, I2=0%).

Conclusion: Based on UE-FM, FIM, and WMFT scores, TVNS combined with rehabilitation training showed some improvement in upper limb motor dysfunction in post-stroke patients, but its long-term effects, stimulation sites, stimulation parameters, combined mode with rehabilitation training, and adverse effects still need further observation.

Registration: PROSPERO: CRD42022312453 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022312453).

Keywords: TVNS, stroke, motor function, systematic review, meta-analysis

Introduction

Stroke is the second leading cause of disability and deadly disease today.[1,2] Stroke often results in multiple functional impairments, of which limb movement disorders are more common than others.It mainly manifests as decreased muscle strength, increased muscle tone or abnormal movement patterns,[3,4] which seriously affect the quality of patients' daily life and bring heavy pressure to society and their families.[5] The muscle on the affected side of the patient is characterized by clumsy and slow movements or loss of limb movement. In addition, because of the reduced bilateral limb synergy, the normal function of a healthy limb may be affected; and over-reliance on the healthy upper limb may lead to disuse of the affected limb or secondary injury from overuse of healthy limb. In recent years, rehabilitation methods for upper limb motor dysfunction have

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been diversified, such as rehabilitation training, neuromodulation techniques, acupuncture and other interventions. However, some of these methods' mechanisms are still unclear. The standard non-invasive neuromodulation techniques such as rTMS and tDCS have a high cost, and require professional institutions and personnel to administer the treatment. It is worth noting that rTMS has a risk of inducing epilepsy. Therefore there are certain limitations in clinical practice.

Transcutaneous vagus nerve stimulation (TVNS), a vagus nerve modulation technique,[6] which achieves non-invasive vagus nerve stimulation by stimulating the auricular vagus nerve (TaVNS) or the cervical vagus nerve (TcVNS), can activate vagally mediated pathways similar to invasive vagus nerve stimulation(VNS).[7] In recent years, VNS and TVNS have been used in treating epilepsy, depression, migraine, tinnitus and other diseases,[8–12] and it also has some research and development in stroke. With the development of modern rehabilitation medicine, the efficacy of VNS in upper limb motor dysfunction after stroke is gradually emerging.[13–15] Current studies on VNS and TVNS are associated with chronic stroke.[16] VNS has been found to improve upper limb motor deficits in post-stroke patients, and this intervention is considered to be largely safe.[14] However, it is difficult to promote it on a large scale due to its high cost, high standard of procedures and potential surgical risks (such as cardiac arrhythmias and vocal cord paralysis).[12,17] On the other hand, recent clinical studies have found that TaVNS combined with rehabilitation can promote upper limb motor dysfunction and improve UE-FM scale scores in patients after chronic stroke.[18] It has been found that stimulation of the vagus nerve in combination with rehabilitation can promote the reorganization process of the motor cortex and enhance neuroplasticity.[19] TaVNS has been shown to increase Growth differentiation factor 11 (GDF11) expression in the peri-infarct cortex.[20] GDF11 is a member of the transforming growth factor-β (TGF-β) superfamily.GDF11 has been shown to increase markers of neurogenesis and angiogenesis to improve neurological function after stroke.[21] These results suggest that TVNS can improve upper limb motor dysfunction after stroke to some extent and may be an adjunctive intervention for recovery of limb function after stroke. As a result, TVNS can become a new intervention for motor sensory rehabilitation during chronic stroke due to its safety, low cost, simplicity and non-invasiveness.[18,22,23] But the novelty of the technique and the fact that the mechanism is still unclear, the clinical efficacy is still controversial and needs further validation. Two previous systematic reviews and meta-analyses have been conducted,[24,25] which consolidated the data from existing clinical studies on VNS for upper limb motor dysfunction after stroke. Both were divided into TVNS and invasive vagus nerve stimulation (iVNS) for subgroup analysis. However, there is a lack of targeted research on TVNS. This study aims to conduct a systematic review of the most recent studies and provide further scientific evidence and data to support the use of TVNS in clinical rehabilitation of post-stroke.

Information and Methods

The systematic review were performed and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-analysis 2020 statement (PRISMA 2020) and Cochrane Review's Handbook 5.1. In addition, this study was registered in the international perspective systematic review register (PROSPERO): CRD42022312453. This study was based on the integration of previously published research data.Therefore, it did not require approval from the ethics review board.

Research Search

This study searched six databases: PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure Database (CNKI), China Science and Technology Journal Database (VIP), and Wanfang Database, with the search period from January 1, 2016 to January 30, 2022. Search terms included keywords associated with stroke, motor function, transcutaneous vagus nerve stimulation and related terms (search strategy of PubMed is presented in Table 1). No restrictions were placed on ethnicity, the language of publication, or the type of journal published.

Inclusion Criteria

Study Type

The study included was a randomized controlled trial, with or without blinding and allocation concealment.

Table 1 Search Strategy of PubMed

PubMed
1. (tavns) OR (tvns) OR (nvns) OR (Transcutaneous auricular vagus nerve stimulation) OR (Transcutaneous vagus nerve stimulation) OR (Noninvasive vagus nerve stimulation)
2. "Stroke"[MeSH Terms]
3. (stroke) OR (Strokes) OR (Cerebrovascular Accident) OR (Cerebrovascular Accidents) OR (Cerebrovascular Accidents) OR (CVA (Cerebrovascular Accident) OR (CVAs (Cerebrovascular Accident)) OR (Cerebrovascular Apoplexy) OR (Apoplexy, Cerebrovascular)) OR (Vascular Accident, Brain)) OR (Brain Vascular Accident) OR (Brain Vascular Accidents) OR (Vascular Accidents, Brain) OR (Cerebrovascular Stroke) OR (Cerebrovascular Strokes) OR (Stroke, Cerebrovascular) OR (Strokes, Cerebrovascular) OR (Apoplexy) OR (Cerebral Stroke) OR (Cerebral Strokes) OR (Stroke, Cerebral) OR (Strokes, Cerebral) OR (Acute Stroke) OR (Acute Strokes) OR (Strokes, Acute) OR (Cerebrovascular Accident, Acute) OR (Acute Cerebrovascular Accident) OR (Acute Cerebrovascular Accidents) OR (Cerebrovascular Accidents, Acute)
4. 2 OR 3
5. (Motor dysfunction) OR (Hhypokinesia) OR (Motor function)
6. 1 AND 4 AND 5

Inclusion

All patients were 18 years of age or older and met the diagnostic criteria for stroke with appropriate imaging such as CT or MRI; they also had upper limb motor dysfunction; there were no restrictions on their age, gender, race, duration of disease, weight or education level.

Interventions

The primary interventions are TVNS combined with rehabilitation, including TaVNS and TcVNS, which can be combined with conventional treatment.

Control Group Measures

Interventions include TVNS sham stimulation, and conventional and appropriate combined treatments.

Outcome Indicators

The primary outcome indicator was the Upper Extremity Fugl-Meyer Score (UE-FM), and secondary outcome indicators included the Wolf Motor Function Test Score(WMFT) and the Function Independent Measure Score (FIM). Studies containing any of these outcome indicators will be included in this systematic review.

Exclusion Criteria

(A) Inclusion of patients with other malignant diseases.
(B) Single-arm tests without controls, animal experiments, case reports, expert experience, and conference papers.
(C) Studies with incomplete data.
(D) Repeated published studies.

Study Data Extraction and Quality Evaluation

Two independent professional reviewers did all study data extraction and quality analysis, and a third reviewer adjudicated the disagreements.

Literature Inclusion

Two reviewers searched relevant literature based on the literature search strategy and then compared and supplemented the results to eliminate duplicate literature via Endnote checking function. Afterwards, two reviewers read the title, abstract and keywords to eliminate literature irrelevant to the study, read the full text according to the Inclusion and exclusion criteria, and finally included the literature that met the criteria in the study.

Data Extraction

Two reviewers designed a standardized data extraction form, which should include basic information about the study (including first author, year of publication), essential demographic characteristics of the intervention population (such as sample size, age, gender, diagnosis, duration of disease), study characteristics (study type, grouping method, blinding, allocation concealment), intervention protocol (intervention type, intervention parameters, intervention period), outcome indicators (such as primary outcome indicators, secondary outcome indicators, follow-up), adverse effects. All outcome indicators are based on data at the end of the intervention and do not include follow-up data.

Quality Assessment

Two independent reviewers evaluated the quality of the included studies using the Cochrane Review's Handbook 5.1 evaluation criteria, containing the following entries: ① randomization method; ② allocation concealment; ③ blinding of subjects and interventionists (implementation bias); ④ blinding of data statisticians (measurement bias); ⑤ data completeness (follow-up bias); ⑥ selective reporting (reporting bias); ⑦ other biases. Above seven items were evaluated on three levels "Low Risk", "Some Concern", and "High Risk". On the other hand, the reviewers used the PEDro scale to evaluate the quality of these studies, consisting of 11 items with a total score of 11. 9–11 points were considered as "excellent" quality, 6–8 as "good" quality, 3–5 as "fair" quality and below three as "poor" quality.[26]

Data Analysis

Handling of Missing Data

For studies with incompletely reported data, reviewers were contacted by email to obtain the complete raw data. If the required amount of changes were not fully reported, reviewers would manually calculate the mean and standard deviation via the Cochrane Handbook formulae based on their reported baseline and outcome data.

Meta-Analysis

All data analyses were performed using Review Manager 5.4.1 software (The Cochrane Collaboration, Copenhagen, Denmark). All outcome indicators included in this study were continuous variables, so mean differences (MD) and corresponding 95% confidence intervals (95% CI) were assessed for the corresponding data. On the other hand, we assessed risk ratios (RRs) at 95% CI for adverse events. Heterogeneity was assessed using the chi-square test and I2. $P<0.05$ or I2 value >50% was considered high heterogeneity, and a random-effects model was used; otherwise, a fixed effects model was used. Heterogeneity used sensitivity and subgroup analysis to identify the source of their heterogeneity. Descriptive analysis was performed if the source of heterogeneity could not be determined. Bias analysis was not performed as too few studies were included in this study ($n<10$).

Results

Research Search

A total of 85 studies were retrieved according to the formulated search strategy. Thirteen duplicate studies were removed through the Endnote software check function. Forty-four studies which were irrelevant to the study, five animal studies and ten reviews, were excluded by reading the titles and abstracts. Four trial protocols, two single-arm pilot studies, one study for which no raw data were available and one retrospective study were excluded by reading the full text based on the exclusion criteria. One study was excluded from this systematic review due to missing data. The final four randomized controlled studies were included,[27–30] of which two were in English[28,30] and two were in Chinese.[27,29] We created a PRISMA flow chart to illustrate the process (Figure 1).

Study Characteristics

Four RCTs were included in this study with 101 samples for this systematic review. The basic information of the included study subjects is shown in Table 2. All samples included in the four studies were patients with chronic stroke.Complete subject information was recorded in all four studies.[27–30] The largest sample size included in the study was 42 cases,[27] and the smallest was 12 cases.[30] The intervention period ranged from 2 to 4 weeks. Three studies had a stimulation

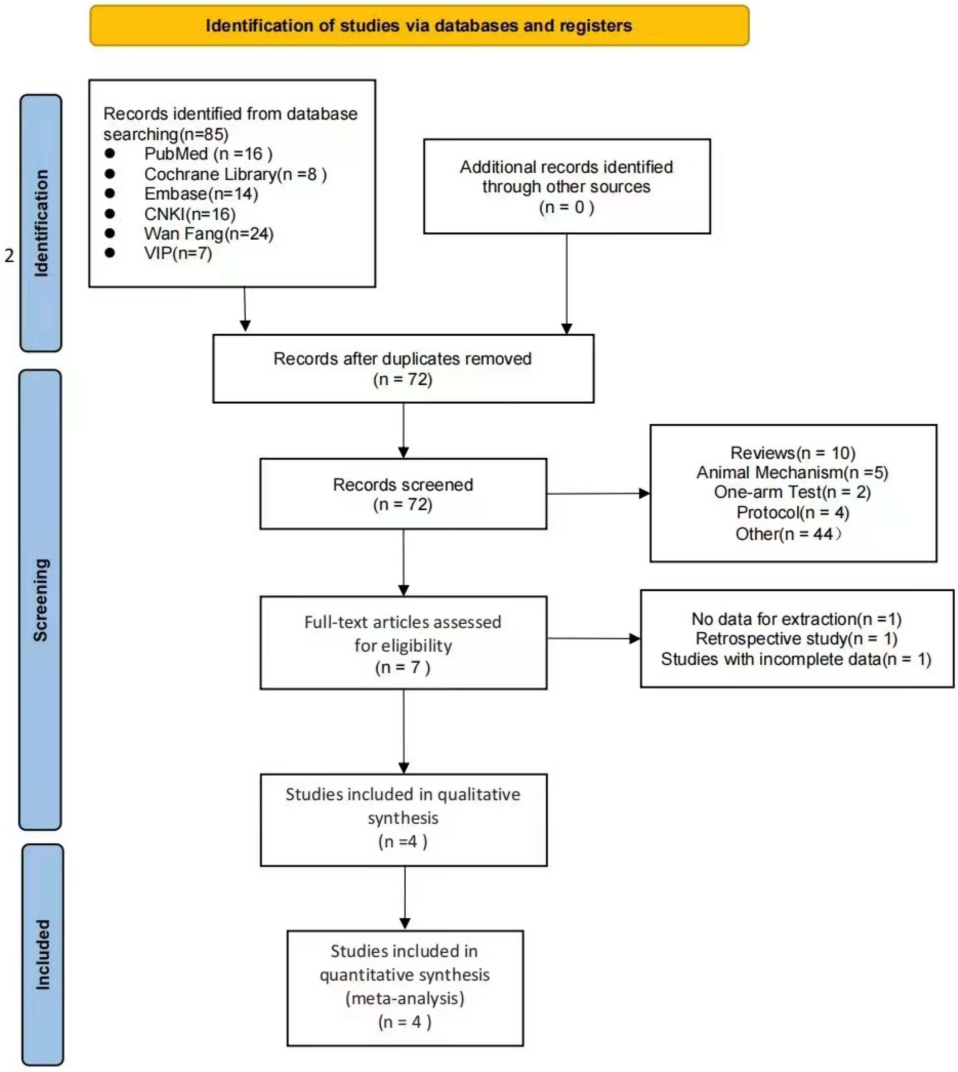

Figure 1 PRISMA flow chart.

frequency of 20 Hz,[27,28,30] one study had a stimulation frequency of 25 Hz.[29] All studies were divided into two groups, the observation group was TaVNS combined with rehabilitation, the control group was stimulated with sham TaVNS combined with rehabilitation, and one study referred to robot-assisted rehabilitation,[30] three studies were conventional rehabilitation.[27–29] In addition, the stimulation site of the four RCTs was the left ear, thus avoiding sinus bradycardia caused by stimulation of the right vagus node.[12] The primary outcome indicator was the UE-FM score in all four studies, and the remaining outcome indicators included the WMFT score, and FIM score. Of the four clinical studies included, one study had TVNS and rehabilitation at the same time,[29] two had not had TVNS and rehabilitation training at the same time,[29,30] while one did not document the specific mode of intervention.[27] Two studies reported adverse events.[28,29] We selected the number of adverse events related to the device, or the treatment process as indicators of TaVNS safety.

Quality Evaluation

Of the four RCTs included in the systematic review, three studies[27–29] reported on the generation of specific randomization methods; one study mentioned allocation concealment.[29] Three studies of RCTs completed subject-blinded,[27,28,30] and one study completed a triple-blind.[27] Two studies recorded follow-up information,[28,29] and all four RCTs completed clinical trials and reported on pre-defined outcome indicators. Two reviewers evaluated the results, and the results of risk of bias assessments are shown in Figures 2 and 3. Finally, three studies[27–29] were found to be at low risk of bias and one

Table 2 Characteristics of Included Studies

Study	Design	TVNS			Sham-TVNS			TVNS Stimulation Parameters						Rehabilitation Training	Main Findings	Follow-Up
		N	Age	Course of Disease	N	Age	Course of Disease	Site	Pulse Width	Frequency	Intensity	Interval	Duration			
Capon 2017[30]	RCT	7	53.71 ±5.88	93.71 ±38.81m	5	55.6 ±7.12	46.00 ±21.85m	Left external acoustic meatus	0.3 ms	20 Hz	2.8–7.2 mA	5 min	60 min/day for ten days	Patients received a session of robotic therapy immediately following the real or sham stimulation.	The mean change in the UE-FM score in the VNS group was 5.4 (SD 2.94) vs 2.8 (SD 3.03) in the control group.	
Zhang 2020[27]	RCT	21	66.10 ±1.491	64.19 ±1.027	21	38.00 ±1.459	36.86 ±1.959	Left cavum concha		20Hz	0.5mA	30 s trains every 2 min	30min/ time,1 time/day, 5 times/ week, continuous treatment for 3 weeks	Patients were treated with true or sham TVNS on the basis of traditional rehabilitation training.	The mean change in the UE-FM score in the VNS group was 5.86 (SD 24.19) vs 3.43 (SD 20.98); The mean change in the FIM score in the VNS group was 9.82 (SD 102.35) vs 6.48 (SD 96.02) in the control group; The mean change in the WMFT score in the VNS group was 5.28 (SD 26.57) vs 2.76 (SD 23.28) in the control group.	
Wei 2020[29]	RCT	13	61.31 ±11.54	48.77 ±24.74	13	57.23 ±10.17	50.38 ±22.07	Left cavum concha	0.1ms	25Hz		30 s trains every 30s	60 min/ time, five times/ week, stimulation four weeks	Traditional rehabilitation training is carried out simultaneously with real or sham taVNS.	The mean change in the UE-FM score in the VNS group was 16.77 (SD 44.04) vs 6.92 (SD 30.58) in the control group.	There were significant differences in the UE-FM scores between the two groups after four weeks of treatment and during follow-up, and T-taVNS group was significantly higher than F-taVNS group.
Wu 2020[28]	RCT	10	64.5 ±9.97	61.82 ±10.63	11	36.3 ±9.23	35.55 ±6.47	Left cavum concha	0.3ms	20 Hz		30 s trains every 5 min	30min/day for 15 days	Conventional rehabilitation training was performed immediately after the end of real or sham taVNS by the same therapists.	The mean change in the UE-FM score in the VNS group was 6.9 (SD 1.85) vs 3.18 (SD 1.17) in the control group; The mean change in the FIM score in the VNS group was 10.5 (SD 4.93) vs 6.64 (SD 2.58) in the control group; The mean change in the WMFT score in the VNS group was 6.5 (SD 2.37) vs 2.91 (SD 1.14) in the control group.	UE-FM scores remained significantly higher at the 4-week and 12-week follow-up after first intervention compared with baseline in both groups, and a significantly greater improvement was evident in taVNS group compared with the sham-taVNS group.

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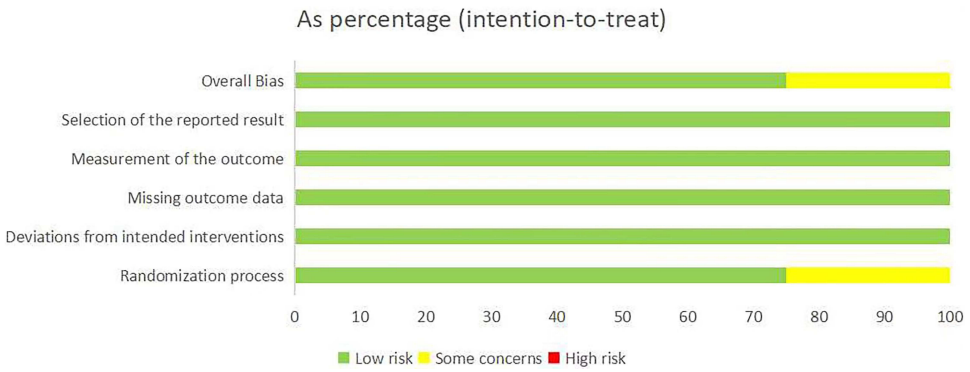

Figure 2 Risk of bias graph of included studies in this systematic review.

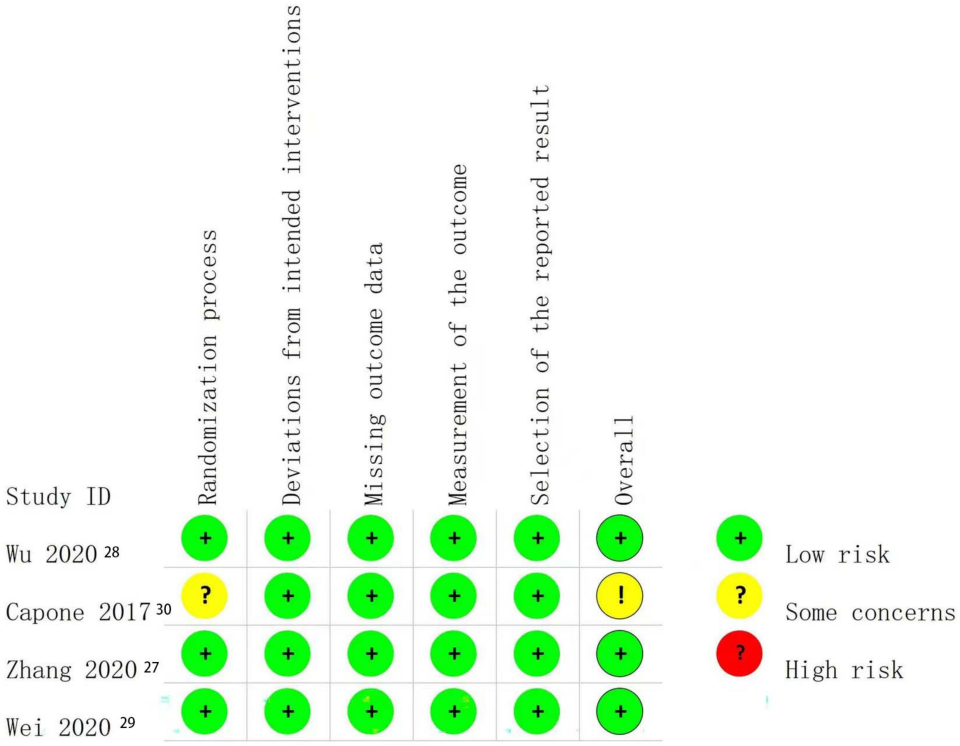

Figure 3 Risk of bias summary of included studies in this systematic review.

study[30] was deemed to have "some concerns" due to concerns about randomisation methods. The PEDro score was used to assess the four RCTs, the results showed that the methodological quality of one study was considered "excellent"[27] and the remaining three studies were rated as "good".[28–30] Details of the assessment are given in Table 3.

Outcome Indicators

The Fugl-Meyer Score for the Upper Limb (UE-FM)

UE-FM were recorded in all four studies, and a fixed effects model was used to integrate the UE-FM data. The results showed a significant difference between the TaVNS group and the sham stimulation group (MD=3.58, 95% CI [2.34, 4.82], P<0.00001), with no heterogeneity found between studies (χ^2=0.54, P=0.91, I2=0%), suggesting that the TaVNS treatment group improved UE-FM significantly superior to the sham stimulation group (Figure 4).

Table 3 PEDro

Study	Inclusion Criteria are Described	Random Allocation	Concealed Allocation	Baseline Comparability	Blind Subjects	Blind Therapists	Blind Assessors	Adequate Follow-Up	Intention-To-Treat Analysis	Between-Group Comparisons	Point Estimates and Variability	Total Score	Quality
Wu 2020[28]	1	0	0	1	1	0	0	1	1	1	1	7	GOOD
Capon 2017[30]	1	0	0	1	1	1	0	1	1	1	0	7	GOOD
Zhang 2020[27]	1	1	0	1	1	1	1	1	1	1	0	9	Excellent
Wei 2020[29]	1	1	1	1	0	0	0	1	1	1	0	7	GOOD

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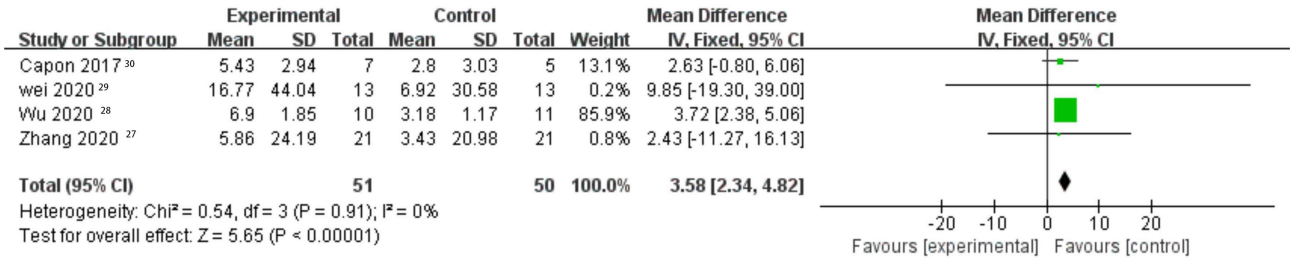

Figure 4 Forest plot of efficacy of VNS on motor function with UE-FM.

Function Independent Measure Score (FIM)

A fixed effects model was used to analyze two FIM scores studies.[27,28] The analysis showed a significant difference in the change in FIM scores between the TaVNS and control groups (MD=3.86, 95% CI [0.45, 7.27], P=0.03), with no heterogeneity was found (χ^2 =0.00, P=0.99, I2=0%), suggesting that the TaVNS treatment group improved FIM significantly better than the sham stimulation group (Figure 5).

Wolf Motor Function Test Score (WMFT)

The WMFT scores of the two studies were analyzed using a fixed effects model.[27,28] The results showed that there was a significant difference in the change in WMFT scores between the TaVNS and control groups (MD=3.58, 95% CI [1.97, 5.18], P<0.0001), and no heterogeneity was found between the studies (χ^2 =0.02, P=0.89, I2=0%), suggesting that the improvement in WMFT in the TaVNS treatment group was significantly better than that in the sham stimulation group (Figure 6).

Safety Evaluation

The primary safety assessment indicators were the number of adverse events during the TVNS intervention. Two studies reported adverse events.[28,29] One patient had redness of the skin at the electrode contact point;[28] one patient had mild nausea and vomiting, and one patient had pain in the left ear.[29] According to simulated result, TVNS is considered generally regarded as safe (Risk Ratio=4.16,95% CI[0.49,34.89], P=0.19), with no heterogeneity (χ^2=0.04, P=0.85, I2=0%), in the intervention of upper limb motor dysfunction after stroke currently (Figure 7).

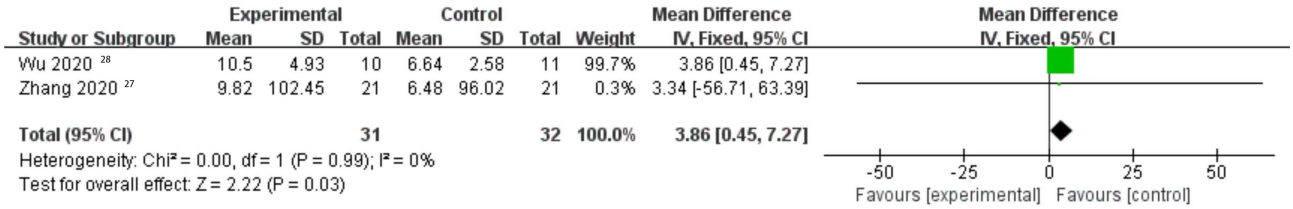

Figure 5 Forest plot for systematic review of efficacy of VNS on motor function with FIM.

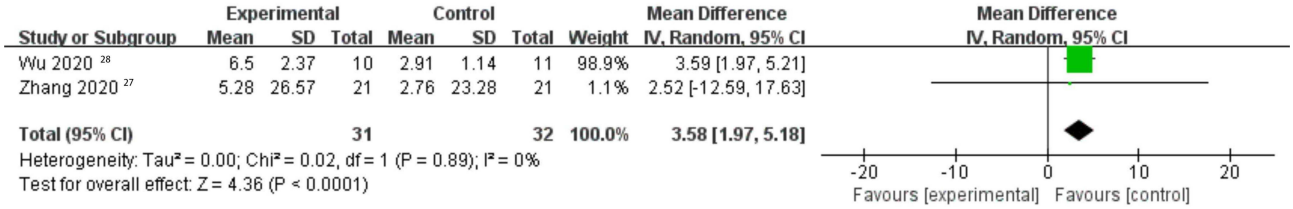

Figure 6 Forest plot for systematic review of efficacy of VNS on motor function with WMFT.

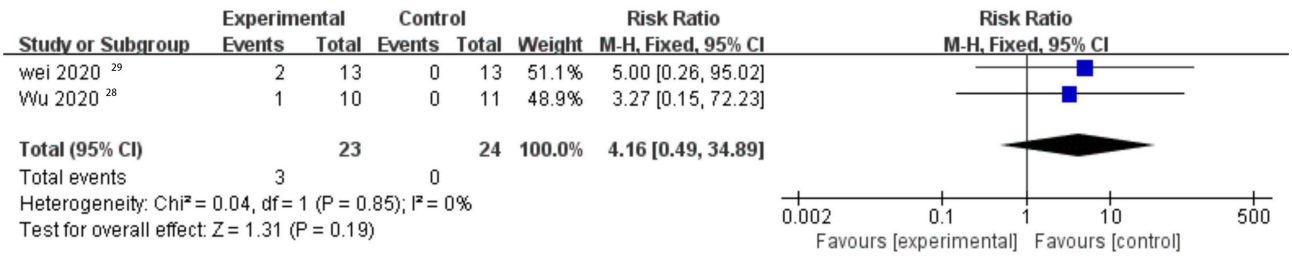

Figure 7 Forest plot for systematic review of efficacy of VNS on safety.

Discussion

This study systematically reviewed all previous clinical studies on TVNS to investigate the effect of TVNS combined with rehabilitation training on upper limb motor dysfunction in post-stroke patients by assessing the clinical efficacy of TVNS through a series of upper limb motor function related scales. In this study, we found that TVNS combined with rehabilitation training can improve upper limb motor dysfunction after stroke. However, all results reported by four studies[27–30] were lower than the minimal important difference, lacked clinical referentiality, and all studies lacked data support from large samples. For the clinical evaluation of TVNS, the flaw is difficult to ignore and would make it difficult to produce high-quality clinical guidance from the results of this systematic review. In addition, level of scales scores flipped between the two groups at follow-up; another study[27] found that the score advantage of the TVNS intervention group diminished over time in the later follow-up of patients, which seems to suggest the issue of the timeliness of the TVNS in the long-term rehabilitation of patients, while also considering whether the problem is related to rehabilitation and other factors during the follow-up period. However, all these studies used TaVNS rather than TcVNS. Therefore, the efficacy of TcVNS for post-stroke upper limb motor dysfunction remains to be investigated in subsequent clinical trials. It is worth mentioning that the site of damage to the stroke lesion and the stroke duration should also be included in later clinical studies, which are essential factors in the outcome of TVNS interventions.

Some basic research has shown that Simultaneous VNS and rehabilitation significantly improved upper limb motor function in MCAO rats, while an efficacy of either rehabilitation alone or VNS and rehabilitation alone was lower than interventions together.[5–7,31] When applied to clinical practice, it is necessary to investigate whether the effects of TVNS, which has a similar mechanism of action to VNS, are linearly correlated with the corresponding rehabilitation programme.

We found that the parameters of the TaVNS intervention varied among the four studies included in this study. As a non-invasive neuromodulation technique, there is no doubt that the effect of the different parameters on the efficacy and their optimization is a goal for future research.

In conclusion, according to the results of the systematic review, TVNS has shown some improvement in upper limb motor dysfunction in patients with chronic-phase stroke and maybe can be used as a clinical adjunct to rehabilitation. However, its long-term effects, stimulation sites, stimulation parameters, combined mode with rehabilitation training and adverse effects still need further observation and research.

Shortcomings in the Study

The clinical studies included in the systematic review were all RCTs, but there are still deficiencies in their blinding and allocation concealment during implementation. Blinding and allocation concealment during the implementation of RCTs is extremely important, which may increase the bias of patient scores or the influence of subjective factors of the participants in the study. That may ultimately reduce the credibility of the study data and further enhance the bias of the systematic review results. However, the current problem is that TVNS as electrical stimulation, particularly TaVNS devices focused on site-specific stimulation, are challenging to implement subject-blinded methods. This deficiency may need to be improved by later improvements in the device or other methods. In clinical RCTs studies, larger samples can provide more reliable data and evidence, while reducing bias in data measurement, which is essential for observing the efficacy of an intervention and can help meta-analyses or systematic reviews to produce more reliable evidence. More importantly, as a newly developed intervention technique, it is important to note the discrepancy between measurements and clinically important differences (CID) in the statistics and observations of clinical studies, as this is a fundamental guarantee of its effectiveness as a clinical intervention.

Conclusion

As a novel non-invasive neuromodulation technology, TVNS is expected to affect upper limb movement disorders in stroke patients. This systematic review showed that TVNS combined with rehabilitation has shown some improvement in upper limb motor deficits in post-stroke patients. However, due to concern about the risk of bias in existing studies, we still do not have sufficient evidence that it can be used as a reliable clinical rehabilitation aid. Further evidence is needed from high-quality studies in the future.

Abbreviations

TVNS, transcutaneous vagus nerve stimulation; VNS, vagus nerve stimulation; iVNS, invasive vagus nerve stimulation; nVNS, noninvasive vagus nerve stimulation; TaVNS, transcutaneous auricular vagus nerve stimulation; TcVNS, transcutaneous cervical vagus nerve stimulation; CNKI, China National Knowledge Infrastructure; VIP, VIP Database for Chinese Technical Periodical; rTMS, repetitive Transcranial Magnetic Stimulation; tDCS, transcranial Direct Current Stimulation; UE-FM, upper extremity Fugl-Meyer; FIM, function independent measure; WMFT, Wolf Motor Function Test; MD, mean differences; CI, confidence intervals; RRs, risk ratios; RCT, randomized controlled trial; CT, computed tomography; MRI, magnetic resonance imaging; MCAO, middle cerebral artery occlusion.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics and Dissemination

Because this is a systematic review, all the data in this study are from published studies and do not involve patients, so there is no need for ethical recognition. The results of this study will be distributed to peer reviews and presented at relevant meetings.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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