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Efficacy evaluation of Buyang Huanwu Decoction in the treatment of ischemic stroke in the recovery period: A systematic review of randomized controlled trials

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Background and purpose: Buyang Huanwu decoction (BYHWD) is widely used in the treatment of ischemic stroke in the recovery period, and many clinical trials have been reported, but its clinical efficacy and safety have not been fully evaluated. In this study, we conducted a systematic review and meta-analysis to evaluate the clinical efficacy and safety of BYHWD in the recovery period.

Materials and methods: Eight databases, including CNKI, Wanfang Database, VIP Database, China Biomedical Literature Database, PubMed, Cochrane Library, EMBASE, and Web of Science, were searched from the establishment of the database to 13 April 2022. We selected all eligible randomized controlled trials of BYHWD in the treatment of ischemic stroke during the recovery period. Systematic review and meta-analysis were conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. The National Institutes of Health Stroke Scale (NIHSS) was the primary outcome, and the Chinese Stroke Scale (CSS), activities of daily living (ADL), and adverse drug reaction (ADR) were the secondary outcomes.

Results: A total of 39 randomized controlled trials were included, and 3,683 patients in the recovery period of ischemic stroke were recruited. Compared with conventional treatment alone, BYHWD combined with conventional treatment significantly decreased the NIHSS score (MD = -1.44, 95% CI: 1.75, -1.12, $p < 0.00001$), the CSS score (MD = -1.18, 95% CI: 2.02, -0.34, $p = 0.006$), improved the ADL (MD = 4.33, 95% CI: 3.06, 5.61, $p < 0.00001$), and

Abbreviations: CT, conventional treatment; NIHSS, National Institute of Health Stroke Scale; CSS, Chinese Stroke Scale; TCM, traditional Chinese medicine; ADL: activities of daily living; ADR, adverse drug reaction; RCT, randomized controlled trial; T/C, treatment group/control group.

did not increase the adverse reactions of patients (OR = 0.88, 95% CI: 0.48, 1.61, $p = 0.67$).

Conclusion: BYHWD is an effective and safe therapy for the recovery of ischemic stroke. To further determine the efficacy and safety of BYHWD in the treatment of ischemic stroke in the recovery period, more high-quality, multicenter, and prospective RCTs are needed.

KEYWORDS

Buyang Huanwu Decoction, ischemic stroke, recovery period, systematic review, meta-analysis, traditional Chinese medicine

1 Introduction

Ischemic stroke is a cerebrovascular disease caused by cerebral ischemia and hypoxia due to cerebral blood supply disorder, resulting in necrosis, softening, and the formation of infarction (Feske, 2021). Ischemic stroke is divided into the acute phase, recovery phase, and sequelae phase. The recovery period refers to 2 weeks to 6 months after the onset of the disease. This period is the key period for the recovery of patients, and it is also an important part of clinical treatment (Belova and Bogdanov, 2021). Patients with ischemic stroke are prone to neurological dysfunction, slow recovery, and many complications, which seriously affect their physical and mental health (Stinear et al., 2020). Active and effective treatments for stroke patients during the recovery period can significantly improve their daily living ability. Besides rehabilitation, antiplatelet aggregation and anticoagulant therapy are commonly used western medicine treatments for these patients, but they easily cause drug resistance and adverse reactions (Boulangier et al., 2018). In recent years, traditional Chinese medicine (TCM) has shown a good effect on ischemic stroke in the recovery period (Guo et al., 2020; Liu, et al., 2021).

Ischemic stroke belongs to the category of “stroke” in TCM. It is mostly caused by deficiency of Qi and blood, lack of nourishment for the brain, block of phlegm and blood stasis, obstruction of brain and collaterals, deficiency of liver and kidney or hyperactivity of liver yang, and disturbance of wind and yang, which in turn causes hemiplegia, skewed tongue, hemianopia, aphasia and other symptoms (Zhao and Zhao, 2021). The main pathogenesis of ischemic stroke is characterized by “wind, fire, phlegm, Qi and blood stasis”. Wang Qingren pioneered the theory of “Qi deficiency and blood stasis” and believed that “the loss of vitality is its source” and “if vitality is deficient, it will not reach the blood vessels. Once the blood vessels have no gas, the blood will stop and become stasis” (Wang, 1999). It should be treated by supplementing qi, activating blood circulation, and removing blood stasis (Zhai et al., 2022). BYHWD is a classical prescription for regulating Qi and blood, removing phlegm and blood stasis in TCM (Shao et al., 2022). It is composed of *Astragalus trimestris* L [Fabaceae, the dried root of *Astragalus trimestris* L]; *Angelica sinensis* (Oliv.) Diels [Apiaceae, the dried

root of *Angelica sinensis* (Oliv.) Diels]; *Paeonia officinalis* subsp. *Officinalis* [Paeoniaceae, the dried root and rhizome of *Paeonia officinalis* subsp. *Officinalis*]; *Pheretima aspergillum* (E. Perrier) [Megascolecidae, the dried body of *Pheretima aspergillum* (E. Perrier)]; *Oreocome striata* (DC.) Pimenov and Kljuykov [Apiaceae, the dried rhizome of *Pheretima aspergillum* (E. Perrier)]; *Oreocome striata* (DC.) Pimenov and Kljuykov]; *Curcuma longa* L [Zingiberaceae, the dried flower of *Curcuma longa* L]; *Prunus persica* (L.) Batsch [the dried seed of *Prunus persica* (L.) Batsch], according to the ratio 120: 6: 5: 3: 3: 3: 3. In a previous study, an HPLC-DAD-ELSD method was developed for simultaneous determination of 12 bioactive compounds in BYHWD, including calycosin-O- β -D-glucoside ononin, calycosin, astragaloside IV and astragaloside I from *Radix Astragalus*; tetramethylpyrazine, ferulic acid and Z-ligustilide from *Radix Angelicae Sinensis* and *Rhizoma Ligustici Chuanxiong*; hydroxysafflor yellow A and kaempferol from *Flos Carthami*; paeoniflorin from *Radix paeoniae Rubra*; and amygdalin from *Semen persicae*. (Liu et al., 2010). In another study, Wang et al. found that hydroxysafflor yellow A, astragaloside IV, ferulic acid, ligustrazine, Z-ligustilide, and linoleic acid were considered to be bioactive compounds of BYHWD (Wang et al., 2021). Kaempferol, Quercetin, Mairin, Jaranol, Hederagenin and AstragalosideIV are the compounds of *Astragalus trimestris* L; Baicalein, Quercetaetin, Beta-carotene, and Baicalin are the compounds of *Paeonia officinalis* subsp. *Officinalis* and *Curcuma longa* L; Ferulic acid and Cis-ligustilide are the compounds of *Angelica sinensis* (Oliv.) Diels; Ligustrazine and Z-ligustilide are the compounds of *Oreocome striata* (DC.) Pimenov and Kljuykov; Sitosterol alpha1 and Folinic acid are the compounds of *Prunus persica* (L.) Batsch; Arachidonic acid and Dihydrocapsaicin are the compounds of *Pheretima aspergillum* (E. Perrier) (Table 1).

Many previous studies have shown that BYHWD has a good therapeutic effect on ischemic stroke. Based on network pharmacology, Wang K et al. found that the active ingredients of Buyang Huanwu Decoction in the treatment of ischemic stroke are baicalein β - Carotene, baicalin, kaempferol, etc. (Wang K, 2021). Cai GX et al. studied the effects of BYHWD on neurological function, quality of life, and serum vascular endothelial growth factor (VEGF) in convalescent patients with

cerebral infarction in a randomized controlled trial (RCT), showing that BYHWD can improve the neurological function and quality of life of convalescent patients with cerebral infarction and increase serum VEGF (Cai and Liu, 2010). Jin C et al. conducted a meta-analysis to evaluate the role of BYHWD in poststroke fatigue patients. The results showed that BYHWD could improve the fatigue severity scale score and the total clinical effective rate (Jin et al., 2021). In recent years, BYHWD has been widely used in the treatment of ischemic stroke in the recovery period, and a large number of clinical trials have described its efficacy and safety, but no rigorous clinical research can provide reliable clinical evidence. The sample size of these trials is generally not large, and it is difficult to convince the public that BYHWD has a significant effect in the treatment of ischemic stroke in the recovery period based on the results of small sample data, which limits the use and promotion of BYHWD to a certain extent. In addition, no systematic review or meta-analysis has focused on the clinical efficacy and safety of BYHWD in the recovery period of ischemic stroke. Therefore, in this study, we conducted a systematic review and meta-analysis to evaluate the clinical efficacy and safety of BYHWD in the recovery period of ischemic stroke.

2 Methods

We conducted this systematic review and meta-analysis in accordance with the PRISMA (preferred Reporting Item for Systematic Reviews and Meta-Analyses) guidelines (Liberati et al., 2009).

2.1 Search strategy

Two independent reviewers (Wang and Ren) searched CNKI, Wanfang Database, VIP Database, China Biomedical Literature Database, PubMed, Cochrane Library, EMBASE, and Web of Science. The last search date was 13 April 2022. The search terms used were (“Apoplexy” OR “Stroke” OR “Cerebral Infarction” OR “Brain Infarction” OR “Ischemic Stroke” OR “Ischemic Apoplexy” OR “Cerebrovascular accident” AND “Buyang Huanwu Decoction” AND “random” OR “randomized controlled trial” OR “controlled clinical trial” OR (RCT) OR (RCT) OR (RCTs). No restrictions were imposed on language or publication status.

2.2 Type of study

2.2.1 Inclusion criteria

1) Type of study: A randomized controlled trial using integrated traditional Chinese and Western medicine in the recovery period of ischemic stroke. The languages are limited to

Chinese and English. 2) Research subjects: patients were diagnosed with ischemic stroke in the recovery period (2 weeks to 6 months after onset). 3) Interventions: The control group received conventional treatment (including controlling blood pressure, improving microcirculation, expanding cerebral vessels, using neurotrophic agents and physical therapy, *etc.* The experimental group was given BYHWD on the basis of conventional treatment. 4) Outcomes: Studies including the National Institute of Health Stroke Scale (NIHSS), Chinese Stroke Scale (CSS), Activities of daily living (ADL), and Adverse drug reaction (ADR).

2.2.2 Exclusion criteria

1) Nonrandomized controlled trials or studies that do not indicate the type of study. 2) The included literature can only extract part of the original data, which makes the data impossible to extract. 3) Animal experiments, literature reviews, conference papers. 4) Outcomes studies that did not include NIHSS, CSS, ADL, and ADR. 5) Studies where interventions did not meet the requirements.

2.3 Participant characteristics

Age, sex, and race were not the limiting conditions for the inclusion criteria. As long as the ischemic stroke patients in the recovery period who met the above criteria were considered to meet the inclusion criteria.

2.4 Interventions

This study selected all RCTs comparing BYHWD with conventional methods in the treatment of ischemic stroke in the recovery period, regardless of language, publication status, or blinding method. Nonrandomized trials, reviews, case reports, and animal studies were excluded. The experimental group used both BYHWD and CT, and the control group used CT alone for comparison. Conventional treatment was the same in both groups.

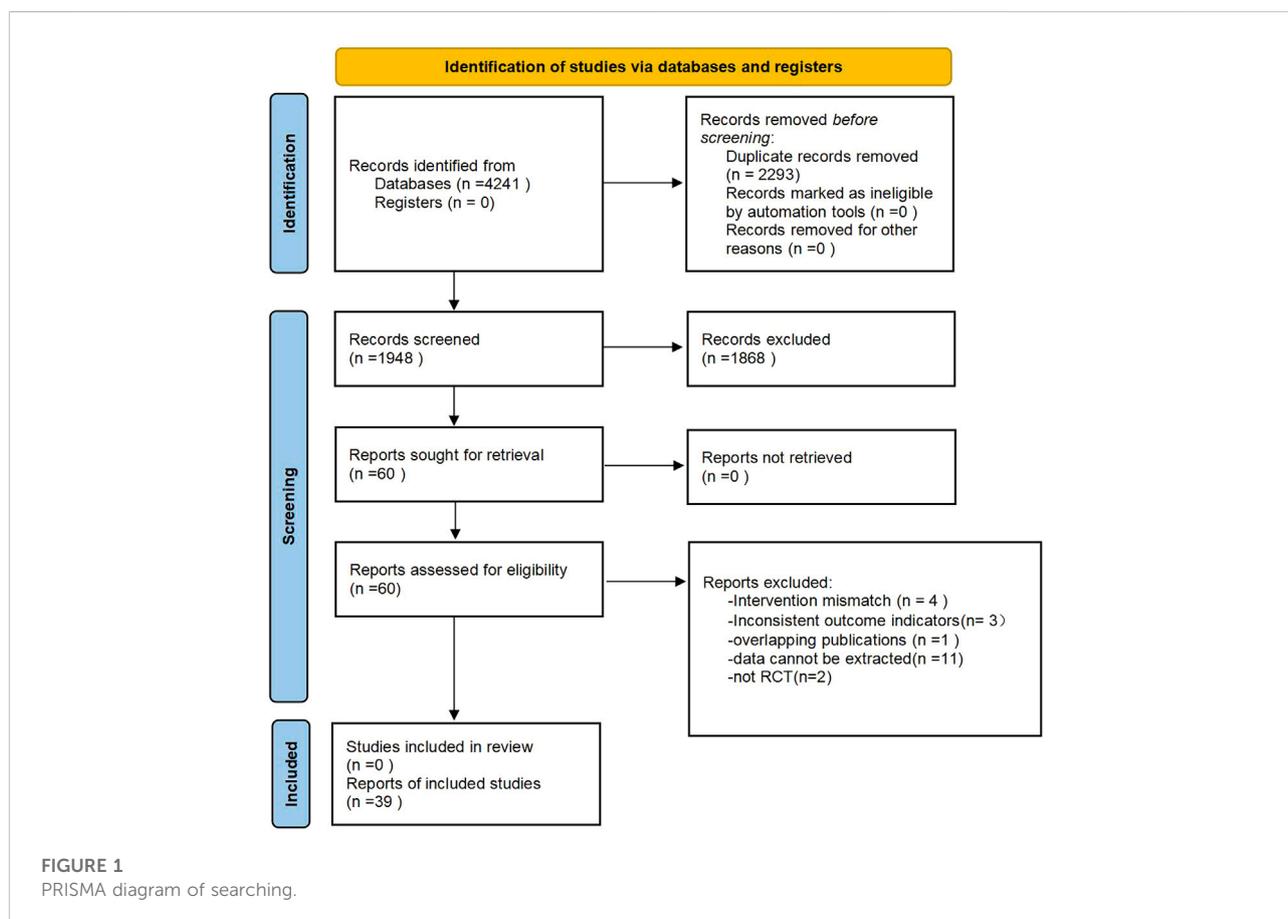
2.5 Outcome measures

The NIHSS was the primary outcome measure, and CSS, ADL, and ADR were the secondary outcomes.

NIHSS (National Institute of Health Stroke Scale) score, which is a quantitative indicator of the severity of AIS disease, is often used as a surrogate endpoint in clinical research and stratifies patients according to the NIHSS score to guide clinical

TABLE 1 Components of buyang huanwu decoction.

| Scientific name | Family | English name | Chinese name | Part used | Quantity (gram) |
|--|----------------|--------------------------------|--------------|------------------|-----------------|
| <i>Astragalus trimestris</i> L | Fabaceae | <i>Astragalus membranaceus</i> | Huang Qi | Root | 120 |
| <i>Angelica sinensis</i> (Oliv.) Diels | Apiaceae | Chinses angelica | Dang Gui | Root | 6 |
| <i>Paeonia officinalis</i> subsp. <i>Officinalis</i> | Paeoniaceae | <i>Paeonia rubra</i> | Chi Shao | Root and rhizome | 5 |
| <i>Pheretima aspergillum</i> (E. Perrier) | Megascolecidae | Earthworm | Di Long | Dried Body | 3 |
| <i>Oreocome striata</i> (DC.) Pimenov and Kljuykov | Apiaceae | Sargentgloryvine | Chuan Xiong | Rhizome | 3 |
| <i>Curcuma longa</i> L | Zingiberaceae | safflower | Hong Hua | Flower | 3 |
| <i>Prunus persica</i> (L.) Batsch | Rosaceae | Peach kernel | Tao Ren | Seed | 3 |



decision-making (Yamal, 2021). It is divided into 11 items, including consciousness, gaze, visual field, facial paralysis, upper limb movement, lower limb movement, ataxia, sensation, language, dysarthria, and neglect, with a score of 0–42. The lower the score, the better the neurological function. The Chinese Stroke Scale (CSS) is based on the standard evaluation of clinical efficacy revised by the fourth national Cerebrovascular Disease Conference (The Fourth National Academic Conference on cerebrovascular disease, 1996). Efficacy standards: A sensory test is performed on the

big toe. Symptom score: yes = 1, no = 0; reflex score: none = 2, diminished = 1L, normal = 0; sensory test score: abnormal = 1, normal = 0. Among them, six points are from symptoms, eight points are from the reflexes of both lower extremities, and five points are from the sensation of the thumbs. The total score is added up, from normal = 0 points to the highest score of 19 points. The patient's ability to do daily living (ADL) was assessed by the Basel index, with a total score of 0–100. A score <40 points indicated that the patient had severe activity disorder; 41–60 points, indicated that the patient needed help to

TABLE 2 Characteristics of studies included in the meta-analysis.

| Serial number | References | Race | Design | Sample size (T/C) | Age (years) (T/C) | Male/female ratio (T; C) | Outcome measure(s) | Interventions | | Treatment duration |
|---------------|------------------------|-----------|--------|-------------------|-------------------------------|--------------------------|--------------------|-----------------|---------------|--------------------|
| | | | | | | | | Treatment group | Control group | |
| 1 | Zuo and Lin (2020) | East Asia | RCT | 50 (25/25) | 67.01 ± 2.13/ 67.21 ± 2.21 | 14/11; 15/10 | NIHSS, CSS, ADL | BYHWD plus CT | CT | 2 weeks |
| 2 | Zhen Jia Quan, 2016 | East Asia | RCT | 98 (49/49) | 56.4 ± 7.6/ 56.8 ± 7.2 | 28/21; 29/20 | CSS, ADL | BYHWD plus CT | CT | 4 weeks |
| 3 | Zhang (2017) | East Asia | RCT | 100 (50/50) | 59.87 ± 4.64/ 60.46 ± 4.92 | 30/20; 31/19 | NIHSS, ADR | BYHWD plus CT | CT | 3 months |
| 4 | Zhang (2013) | East Asia | RCT | 100 (50/50) | 62.7 (45–76) | 53/43 | NIHSS | BYHWD plus CT | CT | 2months |
| 5 | Zhang (2018) | East Asia | RCT | 180 (90/90) | 71.4 ± 4.7 | Not reported | TCM, ADL | BYHWD plus CT | CT | 4 weeks |
| 6 | Zhang and Xiong (2020) | East Asia | RCT | 78 (39/39) | 65.32 ± 5.74/ 65.67 ± 5.21 | 21/18; 20/19 | NIHSS | BYHWD plus CT | CT | 3 months |
| 7 | Yu (2013) | East Asia | RCT | 102 (49/53) | Not reported | Not reported | ADL | BYHWD plus CT | CT | 6months |
| 8 | Yang (2018) | East Asia | RCT | 60 (30/30) | 56.14 ± 3.18/ 55.31 ± 2.27 | 17/13; 16/14 | NIHSS | BYHWD plus CT | CT | 4 weeks |
| 9 | Yang (2020) | East Asia | RCT | 80 (40/40) | 63.25 ± 4.68/ 63.99 ± 4.71 | 24/16; 23/17 | NIHSS | BYHWD plus CT | CT | 4 weeks |
| 10 | Yang et al. (2021) | East Asia | RCT | 90 (45/45) | 58.69 ± 7.52/ 58.72 ± 7.58 | 30/15; 28/17 | NIHSS | BYHWD plus CT | CT | 2months |
| 11 | Xue and Xue (2015) | East Asia | RCT | 74 (36/38) | Not reported | Not reported | CSS | BYHWD plus CT | CT | 15d |
| 12 | Xu et al. (2017) | East Asia | RCT | 170 (85/85) | 65.33 ± 6.72/ 65.16 ± 7.05 | 45/40; 47/38 | TCM, ADL, NIHSS | BYHWD plus CT | CT | 6 weeks |
| 13 | Xu (2014) | East Asia | RCT | 110 (60/50) | 62.1 ± 11.6/ 62.3 ± 10.6 | 37/23; 31/19 | CSS, ADL | BYHWD plus CT | CT | 3 weeks |
| 14 | Xiang (2019) | East Asia | RCT | 60 (30/30) | 64.18 ± 3.44/ 64.24 ± 3.53 | 18/12; 17/13 | NIHSS, ADL | BYHWD plus CT | CT | Not reported |
| 15 | Wu (2021) | East Asia | RCT | 66 (33/33) | 63.35 ± 4.20/ 63.42 ± 4.25 | 18/15; 20/13 | NIHSS, ADL, ADR | BYHWD plus CT | CT | 1month |
| 16 | Wang et al. (2021) | East Asia | RCT | 92 (46/46) | 56.70 ± 5.33/ 56.39 ± 5.50 | 26/20; 27/19 | NIHSS, ADL | BYHWD plus CT | CT | 4 weeks |
| 17 | Wang et al. (2012) | East Asia | RCT | 96 (54/42) | 61.2 ± 11.7/ 62.5 ± 9.6 | 35/19; 22/20 | CSS, ADL | BYHWD plus CT | CT | 4 weeks |
| 18 | Sui (2014) | East Asia | RCT | 120 (60/60) | 63.89 ± 7.05/ 64.06 ± 8.73 | 33/27; 34/26 | NIHSS | BYHWD plus CT | CT | 60d |
| 19 | Shi (2016) | East Asia | RCT | 60 (30/30) | 61.84 ± 3.13/ 61.25 ± 3.22 | 17/13; 18/12 | ADR | BYHWD plus CT | CT | 4 weeks |
| 20 | Shang (2021) | East Asia | RCT | 72 (36/36) | 59.63 ± 7.32/ 58.76 ± 7.45 | 23/13; 20/16 | NIHSS, ADL | BYHWD plus CT | CT | 14d |
| 21 | Meng et al. (2014) | East Asia | RCT | 120 (60/60) | 64.58 ± 7.63/ 65.37 ± 7.80 | 36/24; 33/27 | ADL | BYHWD plus CT | CT | 3 weeks |
| 22 | Liu (2018) | East Asia | RCT | 30 (15/15) | 62.7 ± 4.5/ 63.1 ± 4.2 | 8/7; 9/6 | NIHSS | BYHWD plus CT | CT | 21d |
| 23 | Lin (2014) | East Asia | RCT | 84 (41/43) | Not reported | Not reported | ADL, ADR | BYHWD plus CT | CT | 12 weeks |
| 24 | Li (2012) | East Asia | RCT | 130 (65/65) | 61.3 ± 10.8/ 61.1 ± 11.2 | 35/15; 36/14 | CSS | BYHWD plus CT | CT | 4 weeks |
| 25 | Li (2018) | East Asia | RCT | 70 (35/35) | 61.8 ± 5.3/ 62.3 ± 5.1 | 19/16; 18/17 | NIHSS | BYHWD plus CT | CT | 30d |

(Continued on following page)

TABLE 2 (Continued) Characteristics of studies included in the meta-analysis.

| Serial number | References | Race | Design | Sample size (T/C) | Age (years) (T/C) | Male/female ratio (T; C) | Outcome measure(s) | Interventions | | Treatment duration |
|---------------|----------------------|-----------|--------|-------------------|-------------------------------|--------------------------|--------------------|-----------------|---------------|--------------------|
| | | | | | | | | Treatment group | Control group | |
| 26 | Li and Wei (2021) | East Asia | RCT | 78 (39/39) | 69.32 ± 5.66/ 68.95 ± 5.53 | 29/10; 28/11 | NIHSS, ADL | BYHWD plus CT | CT | 2 weeks |
| 27 | Li (2014) | East Asia | RCT | 84 (41/43) | Not reported | Not reported | ADL, ADR | BYHWD plus CT | CT | 12 weeks |
| 28 | Li (2011) | East Asia | RCT | 61 (31/30) | 45–70/47–72 | 21/10; 19/11 | NIHSS | BYHWD plus CT | CT | 14d |
| 29 | Li (2019) | East Asia | RCT | 84(42/42) | 54.34 ± 8.22/ 54.52 ± 8.16 | 23/19; 24/18 | NIHSS, ADL, ADR | BYHWD plus CT | CT | 4 weeks |
| 30 | Li and Li (2010) | East Asia | RCT | 112(56/56) | 59.1 ± 5.1/ 57.9 ± 6.5 | 31/25; 30/26 | NIHSS, ADL, ADR | BYHWD plus CT | CT | 30d |
| 31 | Jin and Xu (2019) | East Asia | RCT | 60(30/30) | 60.3 ± 7.2/ 58.6 ± 7.5 | 18/12; 16/14 | NIHSS | BYHWD plus CT | CT | 2months |
| 32 | Jiang (2019) | East Asia | RCT | 100(50/50) | 57.9 ± 1.1/ 57.8 ± 1.2 | 28/22; 29/21 | NIHSS | BYHWD plus CT | CT | 4 weeks |
| 33 | Ji (2016) | East Asia | RCT | 60(30/30) | 73.1 ± 11.9/ 72.5 ± 1.25 | 17/13; 18/12 | ADL,ADR | BYHWD plus CT | CT | 4 weeks |
| 34 | Han (2014) | East Asia | RCT | 80(40/40) | 64.58 ± 7.63/ 65.37 ± 7.80 | 36/24; 33/27 | CSS, ADL | BYHWD plus CT | CT | 4 weeks |
| 35 | Fang et al. (2019) | East Asia | RCT | 76 (38/38) | 66.5 ± 4.5/ 65.9 ± 5.2 | 20/18; 24/14 | NIHSS | BYHWD plus CT | CT | 4 weeks |
| 36 | Du (2018) | East Asia | RCT | 90(45/45) | 65.18 ± 2.24/ 65.12 ± 2.13 | 23/22; 24/21 | CSS, ADR | BYHWD plus CT | CT | 4 weeks |
| 37 | Diao (2017) | East Asia | RCT | 60(30/30) | 64.15 ± 5.65/ 63.45 ± 5.15 | 20/10; 20/10 | NIHSS | BYHWD plus CT | CT | 2months |
| 38 | Chen Yan, 2016 | East Asia | RCT | 70(35/35) | 42–75 | 39/31 | ADL | BYHWD plus CT | CT | 8 weeks |
| 39 | Chen Xiao Bing, 2018 | East Asia | RCT | 376(188/188) | 60.2 ± 8.3/ 111 ± 77 | 112/76 | NI HSS, ADL | BYHWD plus CT | CT | Not reported |

Notes: 1. RCT: randomized controlled trial; 2. T/C: Treatment group/control group; 3. NIHSS: national institute of health stroke scale; CSS: cincinnati stroke scale; ADL: activities of daily living; ADR: adverse drug reaction; 4. INTERVENTION STUDY; treatment group; BYHWD, buyang huanwu decoction or modified buyang huanwu decoction; 5. Control group: CT, conventional treatment (including controlling blood pressure, improving microcirculation, expanding cerebral vessels, using neurotrophic agents and physical therapy).

complete daily activities. 60 points meant that the patient needed some help to complete daily activities. The higher the score, the stronger the ADL (Strini et al., 2020). Adverse drug reaction (ADR) mainly referred to gastrointestinal reactions after taking drugs, such as nausea and retching. The internal consistency reliability of NIHSS, CSS, and ADL was high, and the three scales had common validity, but the predictive validity of CSS and ADL was not as comprehensive as NIHSS (Wang et al., 1999; Wu, 2007; Tao 2009).

2.6 Data extraction

Two researchers (Wang and ren) independently screened the literature in strict accordance with the inclusion and exclusion criteria. First, the literature was initially screened by reading the title and abstract and then further screened by reading the full

text. In case of disagreement, a third party (Wu and Zhang) judged, and finally decided to include or exclude through discussion. Then, two researchers (Li and Bai) independently extracted and included relevant research data, including title, author, year, country, diagnosis method of ischemic stroke, the sample size of each group, age, sex, treatment method, treatment time, outcome indicators and evaluation methods, and main research results.

2.7 Methodological quality assessment

The authenticity of the RCTs was assessed by two investigators (Guo and Bai) according to the Cochrane Handbook, and the risk of bias in the literature was assessed according to the Cochrane Risk of Bias Tool. In case of disagreement, a third party (Zhang and Yang) was consulted.

TABLE 3 The methodological quality of the included trials assessed using the Cochrane Risk of Bias Tool.

| Serial number | References | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other bias |
|---------------|------------------------|----------------------------|------------------------|--|--------------------------------|-------------------------|---------------------|------------|
| 1 | Zuo and Lin (2020) | + | + | ? | ? | + | + | + |
| 2 | Zhen Jia Quan, 2016 | ? | + | ? | ? | + | + | + |
| 3 | Zhang (2017) | ? | + | ? | ? | + | + | + |
| 4 | Zhang (2013) | ? | + | ? | ? | + | + | + |
| 5 | Zhang (2018) | + | + | ? | ? | + | + | + |
| 6 | Zhang and Xiong (2020) | ? | + | ? | ? | + | + | + |
| 7 | Yu (2013) | ? | + | ? | ? | - | + | + |
| 8 | Yang (2018) | ? | + | ? | ? | + | + | + |
| 9 | Yang (2020) | + | + | ? | ? | + | + | + |
| 10 | Yang et al. (2021) | ? | + | ? | ? | + | + | + |
| 11 | Xue and Xue (2015) | ? | + | ? | ? | + | + | + |
| 12 | Xu et al. (2017) | + | + | ? | ? | + | + | + |
| 13 | Xu (2014) | ? | + | ? | ? | + | + | + |
| 14 | Xiang (2019) | + | + | ? | ? | + | + | + |
| 15 | Wu (2021) | + | + | ? | ? | + | + | + |
| 16 | Wang et al. (2021) | + | + | ? | ? | + | + | + |
| 17 | Wang et al. (2012) | ? | + | ? | ? | + | + | + |
| 18 | Sui (2014) | + | + | ? | ? | + | + | + |
| 19 | Shi (2016) | + | + | ? | ? | + | + | + |
| 20 | Shang (2021) | ? | + | ? | ? | + | + | + |
| 21 | Meng et al. (2014) | + | + | ? | ? | + | + | + |
| 22 | Liu (2018) | ? | + | ? | ? | + | + | + |
| 23 | Lin (2014) | ? | + | ? | ? | - | + | + |
| 24 | Li (2012) | ? | + | ? | ? | + | + | + |
| 25 | Li (2018) | ? | + | ? | ? | + | + | + |
| 26 | Li and Wei (2021) | + | + | ? | ? | + | + | + |
| 27 | Li (2014) | ? | + | ? | ? | - | + | + |
| 28 | Li (2011) | ? | + | ? | ? | + | + | + |
| 29 | Li (2019) | + | + | ? | ? | + | + | + |
| 30 | Li and Li (2010) | ? | + | ? | ? | + | + | + |
| 31 | Jin and Xu (2019) | ? | + | ? | ? | + | + | + |
| 32 | Jiang (2019) | + | + | ? | ? | + | + | + |
| 33 | Ji (2016) | + | + | ? | ? | + | + | + |
| 34 | Han (2014) | + | + | ? | ? | + | + | + |
| 35 | Fang et al. (2019) | + | + | ? | ? | + | + | + |
| 36 | Du (2018) | + | + | ? | ? | + | + | + |
| 37 | Diao (2017) | ? | + | ? | ? | + | + | + |
| 38 | Chen and Cao (2016) | + | + | ? | ? | + | + | + |
| 39 | Chen and Zhao (2018) | ? | + | ? | ? | + | + | + |

+ = low risk of bias; ? = unclear risk of bias; - = high risk of bias.

The risk of bias was assessed using seven criteria, including random sequence generation, concealed assignment, blinding of participants and personnel, incomplete outcome data, selective reporting, and other biases. The risk of bias was classified into

three categories: “low” (+), “high” (-), and “unclear” (?). The Jadad scale quality score was used to evaluate the methodological quality of the literature, with one to two points for low quality and three to five points for high quality.

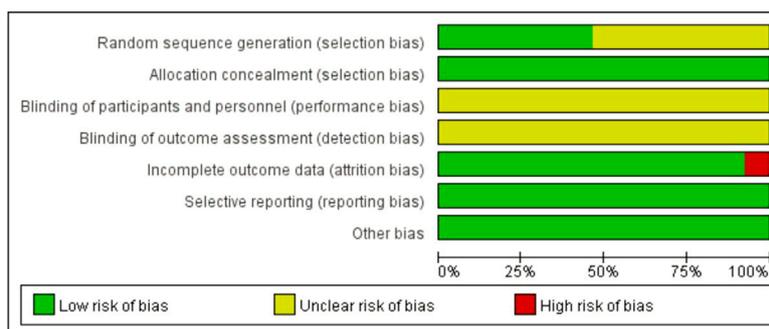


FIGURE 2
Risk of bias graph.

2.8 Data synthesis and analysis

Revman 5.4 software was used for meta-analysis (Copenhagen: the Nordic Cochrane Centre, the Cochrane Collaboration, 2014). Pooled effect size: Count data and measurement data were analyzed by odds ratio (OR), relative risk (RR), mean difference (MD), or standard mean difference (SMD). Heterogeneity analysis: I^2 was used to assess the heterogeneity of the studies. When $I^2 < 50\%$, $p > 0.1$, it indicated that the heterogeneity was not significant, and a fixed effect model was used; when $I^2 \geq 50\%$, $p \leq 0.1$, it indicated that the heterogeneity was substantial, and the source of heterogeneity needed to be analyzed. If there was substantial heterogeneity, a random effect model was used (Cumpston and Li, 2019; Wang et al., 2019; Chen H. et al., 2020; Wu et al., 2020); if the heterogeneity still existed, the source of heterogeneity was analyzed from both methodological and clinical aspects, and subgroup analysis was used.

2.9 Risk of bias across trials

Funnel plots and Egger's test were carried out to examine the potential bias in the included trials when the number of RCTs was ≥ 10 (Egger et al., 1997; Wu et al., 2020).

2.10 Quality of evidence

Two independent reviewers (Wang and Ren) used the GRADE (grading of recommendations, assessment, development, and evaluations) method (Guyatt et al., 2008) to evaluate the risk of bias in each included trial. If there was disagreement on the downgrade or upgrade evaluation, it was evaluated and decided by the third party (Wu and Zhang). Evidence evaluation adopts four grades of "high", "medium", "low" and "extremely low".

3 Results

3.1 Study identification and selection

After searching major databases, a total of 4,241 articles were retrieved. A total of 2294 duplicates were excluded, and 1948 remained; 1868 were excluded after reading the title and abstract, and 60 remained; 21 were excluded after reading the full text, and 39 were finally included in the study. Figure 1 shows the general flow of the study selection process. Table 2 summarizes the general characteristics of the 39 studies.

3.2 Risk of bias

The risks of bias in the trials are shown in Table 3 and Figure 2, and Figure 3. All 39 trials included in this study explicitly used random sequence generation, of which 18 described the randomization methods in detail (random number table method for 16 trials: Liang et al., 2021; Yang 2022; Zuo and Lin, 2020; Zhang, 2018; Xu et al., 2017; Xiang, 2019; Wu, 2021; Wang et al., 2021; Sui, 2014; Shi, 2016; Li and Wei, 2021; Li, 2019; Jiang, 2019; Ji, 2016; Han, 2014; Fang et al., 2019; Chen and Cao, 2016; random alphabet method for one trial: (Meng et al., 2014); random envelope method for one trial: (Du, 2018). The other 21 articles described the use of randomization but did not provide detailed information on the methods of randomization.

Based on the information from the included literature, all the studies performed allocation concealment. The blinding of participants or personnel and the blinding of outcome assessments were not mentioned in any of the studies. Detection bias on complete outcome data was considered low in all trials. All data were also considered to be at low risk of selective reporting and other biases.

| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|-----------------------|---|---|---|---|--|--------------------------------------|------------|
| chen xiao bing2018 | ? | ? | ? | ? | ? | ? | ? |
| chen yan2016 | ? | ? | ? | ? | ? | ? | ? |
| diao li dan2017 | ? | ? | ? | ? | ? | ? | ? |
| du quan jun2018 | ? | ? | ? | ? | ? | ? | ? |
| fang tao2019 | ? | ? | ? | ? | ? | ? | ? |
| han shaung2014 | ? | ? | ? | ? | ? | ? | ? |
| jiang pin li2019 | ? | ? | ? | ? | ? | ? | ? |
| jin dan2019 | ? | ? | ? | ? | ? | ? | ? |
| ji xiao li2016 | ? | ? | ? | ? | ? | ? | ? |
| li can hui2010 | ? | ? | ? | ? | ? | ? | ? |
| li dong yan2019 | ? | ? | ? | ? | ? | ? | ? |
| li guo qing2011 | ? | ? | ? | ? | ? | ? | ? |
| lin xin e2014 | ? | ? | ? | ? | ? | ? | ? |
| li run sheng2014 | ? | ? | ? | ? | ? | ? | ? |
| li shi yin2021 | ? | ? | ? | ? | ? | ? | ? |
| li tie jun2018 | ? | ? | ? | ? | ? | ? | ? |
| liu dong hui2018 | ? | ? | ? | ? | ? | ? | ? |
| li xin hua2012 | ? | ? | ? | ? | ? | ? | ? |
| meng wei2014 | ? | ? | ? | ? | ? | ? | ? |
| shang hai ping2021 | ? | ? | ? | ? | ? | ? | ? |
| shi wen hua2016 | ? | ? | ? | ? | ? | ? | ? |
| sui wen le2014 | ? | ? | ? | ? | ? | ? | ? |
| wang hen2012 | ? | ? | ? | ? | ? | ? | ? |
| wang xin2021 | ? | ? | ? | ? | ? | ? | ? |
| wu jian po2021 | ? | ? | ? | ? | ? | ? | ? |
| xiang jie xiang2019 | ? | ? | ? | ? | ? | ? | ? |
| xue li li2015 | ? | ? | ? | ? | ? | ? | ? |
| xu guo dong2014 | ? | ? | ? | ? | ? | ? | ? |
| xu hui2017 | ? | ? | ? | ? | ? | ? | ? |
| yang jin ping2021 | ? | ? | ? | ? | ? | ? | ? |
| yang su ting2020 | ? | ? | ? | ? | ? | ? | ? |
| yang yin2018 | ? | ? | ? | ? | ? | ? | ? |
| yu feng shen2013 | ? | ? | ? | ? | ? | ? | ? |
| zhang gui xian2020 | ? | ? | ? | ? | ? | ? | ? |
| zhang jun liang 2018 | ? | ? | ? | ? | ? | ? | ? |
| zhang liang shan 2013 | ? | ? | ? | ? | ? | ? | ? |
| zhang min wang 2017 | ? | ? | ? | ? | ? | ? | ? |
| zhen jia quan 2016 | ? | ? | ? | ? | ? | ? | ? |
| zuo quan ting 2020 | ? | ? | ? | ? | ? | ? | ? |

FIGURE 3 Risk of bias summary.

In addition, the Jadad scale quality score is shown in Table 4. The final scores of 39 articles were all three or above, belonging to high-quality literature.

3.3 Outcome measures

The summary of the meta-analysis is presented in Table 5.

3.4 Primary outcome

3.4.1 NIHSS

Twenty-three articles reported the NIHSS scores of patients after BYHWD combined with conventional treatment or conventional treatment alone. Due to the results of the heterogeneity test among the studies ($p = 1.00, I^2 = 0\%$), a fixed effect model was used. The results of the meta-analysis showed that the NIHSS score of the experimental group was significantly lower than that of the control group (MD = -1.44%, 95% CI: 1.75, -1.12, $p < 0.00001$) (Figure 4).

3.5 Secondary outcomes

3.5.1 CSS

Six articles reported the CSS of patients after different treatments with BYHWD plus conventional treatment or conventional treatment alone. There was no heterogeneity among the studies ($p = 0.95, I^2 = 0\%$), and a fixed effect model was used. The results of the meta-analysis showed that the CSS score of the experimental group was statistically lower than that of the control group (MD = -1.18, 95% CI: 2.02, -0.34, $p = 0.006$) (Figure 5).

3.6 ADL

The results of the meta-analysis showed that compared with the control group, the ADL of patients in the experimental group was significantly improved (MD = 4.33, 95% CI: 3.06, 5.61, $p < 0.00001$) (Figure 6).

3.8 ADR

The results of the meta-analysis showed that compared with conventional treatment alone, BYHWD plus conventional treatment did not increase the adverse reactions of patients (OR = 0.88, 95% CI: 0.48, 1.61, $p = 0.67$) (Figure 7).

TABLE 4 The methodological quality of the included trials assessed using the Jadad scale quality score.

| Serial number | References | Random sequence generation | Double-blind method | Withdrawals and missed visits | Score |
|---------------|------------------------|----------------------------|---------------------|-------------------------------|-------|
| 1 | Zuo and Lin (2020) | 2 | 1 | 1 | 4 |
| 2 | Zhen Jia Quan, 2016 | 1 | 1 | 1 | 3 |
| 3 | Zhang (2017) | 1 | 1 | 1 | 3 |
| 4 | Zhang (2013) | 1 | 1 | 1 | 3 |
| 5 | Zhang (2018) | 2 | 1 | 1 | 4 |
| 6 | Zhang and Xiong (2020) | 1 | 1 | 1 | 3 |
| 7 | Yu (2013) | 1 | 1 | 1 | 3 |
| 8 | Yang (2018) | 1 | 1 | 1 | 3 |
| 9 | Yang (2020) | 2 | 1 | 1 | 4 |
| 10 | Yang et al. (2021) | 1 | 1 | 1 | 3 |
| 11 | Xue and Xue (2015) | 1 | 1 | 1 | 3 |
| 12 | Xu et al. (2017) | 2 | 1 | 1 | 4 |
| 13 | Xu (2014) | 1 | 1 | 1 | 3 |
| 14 | Xiang (2019) | 2 | 1 | 1 | 4 |
| 15 | Wu (2021) | 2 | 1 | 1 | 4 |
| 16 | Wang et al. (2021) | 2 | 1 | 1 | 4 |
| 17 | Wang et al. (2012) | 1 | 1 | 1 | 3 |
| 18 | Sui (2014) | 2 | 1 | 1 | 4 |
| 19 | Shi (2016) | 2 | 1 | 1 | 4 |
| 20 | Shang (2021) | 1 | 1 | 1 | 3 |
| 21 | Meng et al. (2014) | 2 | 1 | 1 | 4 |
| 22 | Liu (2018) | 1 | 1 | 1 | 3 |
| 23 | Lin (2014) | 1 | 1 | 1 | 3 |
| 24 | Li (2012) | 1 | 1 | 1 | 3 |
| 25 | Li (2018) | 1 | 1 | 1 | 3 |
| 26 | Li and Wei (2021) | 2 | 1 | 1 | 4 |
| 27 | Li (2014) | 1 | 1 | 1 | 3 |
| 28 | Li (2011) | 1 | 1 | 1 | 3 |
| 29 | Li (2019) | 2 | 1 | 1 | 4 |
| 30 | Li and Li (2010) | 1 | 1 | 1 | 3 |
| 31 | Jin and Xu (2019) | 1 | 1 | 1 | 3 |
| 32 | Jiang (2019) | 2 | 1 | 1 | 4 |
| 33 | Ji (2016) | 2 | 1 | 1 | 4 |
| 34 | Han (2014) | 2 | 1 | 1 | 4 |
| 35 | Fang et al. (2019) | 2 | 1 | 1 | 4 |
| 36 | Du (2018) | 2 | 1 | 1 | 4 |
| 37 | Diao (2017) | 1 | 1 | 1 | 3 |
| 38 | Chen and Cao (2016) | 2 | 1 | 1 | 4 |
| 39 | Chen and Zhao (2018) | 1 | 1 | 1 | 3 |

1–2 points for low quality; three to five points for high quality.

3.9 Publication bias

The funnel plots of the NIHSS suggested that there was a possible publication bias in small trials (Figure 8). Egger's test also indicated there was significant publication bias ($p = 0.672$).

3.10 Quality of evidence

Using GRADE, we assessed the certainty of the evidence to be moderate to low for outcomes for which data were available. In all 39 trials, the quality of evidence was downgraded by one level

TABLE 5 Summary of the meta-analysis.

| Outcome or subgroup | No. Of studies | No. Of participants | Statistical method | Effect size | p |
|---|----------------|---------------------|---------------------|----------------------|-----------|
| Adverse drug reaction | 12 | 956 | RR (fixed), 95% CI | 0.88 [0.50, 1.57] | 0.67 |
| | | | OR (fixed), 95% CI | 0.88 [0.48, 1.61] | 0.67 |
| | | | RD (fixed), 95% CI | -0.01 [-0.03, 0.02] | 0.68 |
| Activities of daily living | 20 | 2194 | SMD (fixed), 95% CI | 0.27 [0.19, 0.36] | <0.00001a |
| | | | WMD (fixed), 95% CI | 4.33 [3.06, 5.61] | <0.00001a |
| National Institute of Health Stroke Scale | 23 | 2121 | SMD (fixed), 95% CI | -0.38 [-0.47, -0.29] | <0.00001a |
| | | | WMD (fixed), 95% CI | -1.44 [-1.75, -1.12] | <0.00001a |
| Cincinnati Stroke Scale | 6 | 568 | SMD (fixed), 95% CI | -0.23 [-0.39, -0.06] | 0.007a |
| | | | WMD (fixed), 95% CI | -1.18 [-2.02, -0.34] | 0.006a |

^aThe treatment group had significantly improved outcomes.

OR, odds ratio; RD, risk difference; RR, relative ratio; SMD, standardized mean difference; WMD, weighted mean difference.

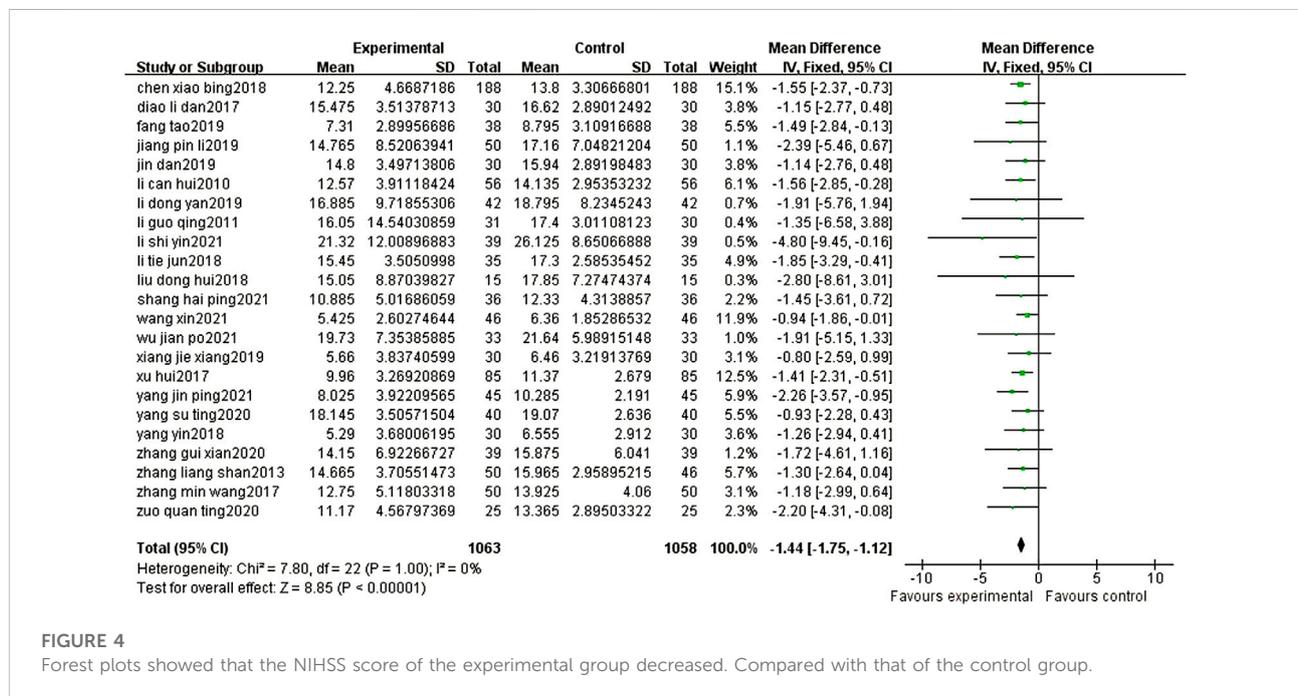


FIGURE 4

Forest plots showed that the NIHSS score of the experimental group decreased. Compared with that of the control group.

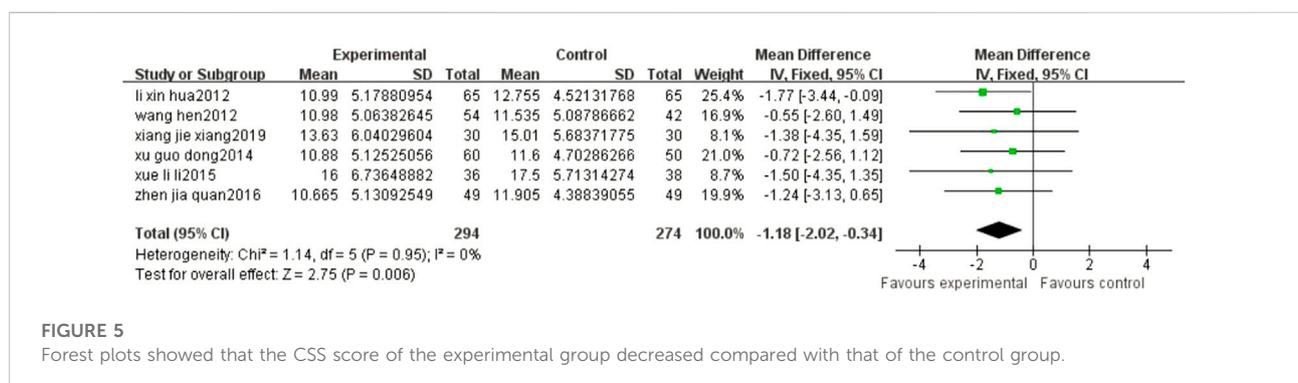


FIGURE 5

Forest plots showed that the CSS score of the experimental group decreased compared with that of the control group.

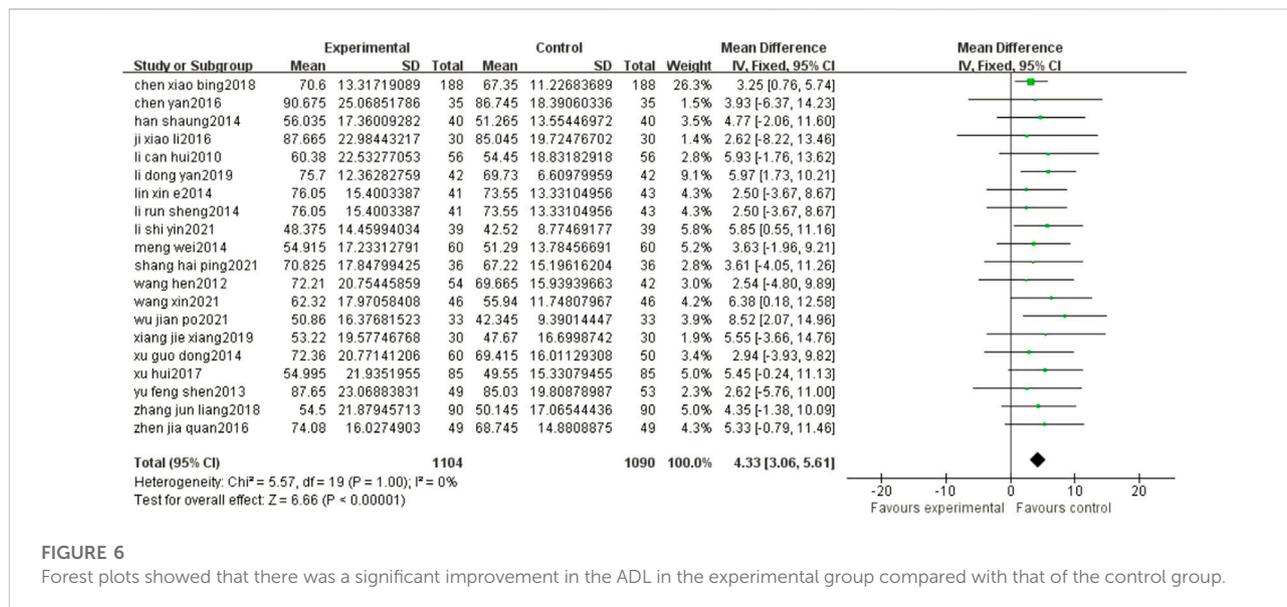


FIGURE 6 Forest plots showed that there was a significant improvement in the ADL in the experimental group compared with that of the control group.

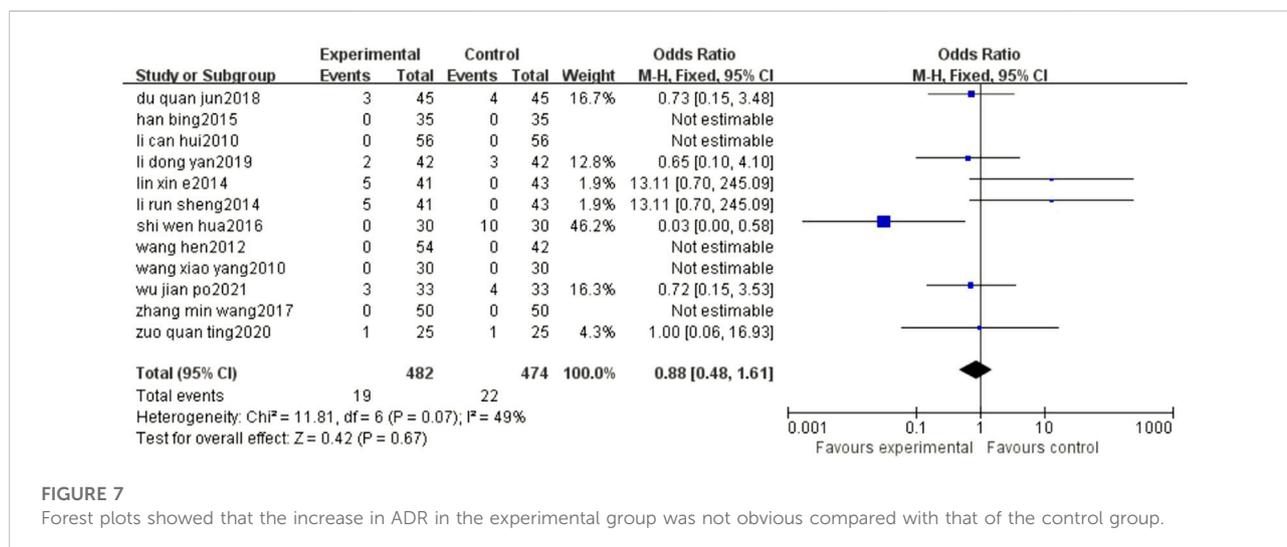


FIGURE 7 Forest plots showed that the increase in ADR in the experimental group was not obvious compared with that of the control group.

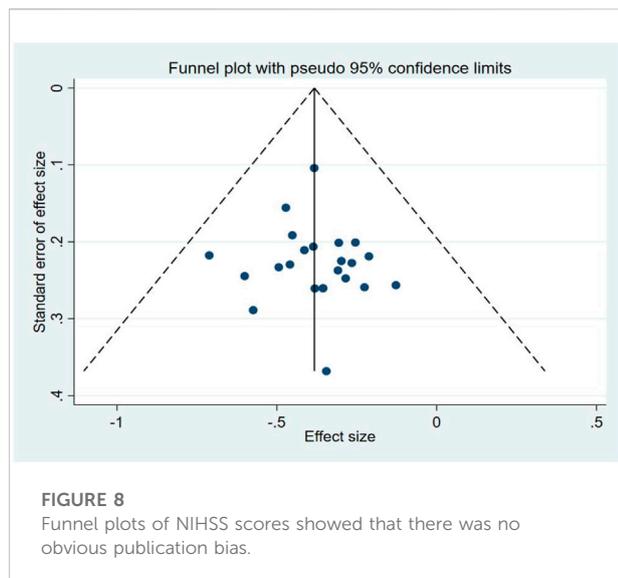
because of the unclear risk of method bias in some trials. The total number of patients was enough for each outcome, and the statistical heterogeneity of the results was small, so the quality of evidence for these outcomes was upgraded by one level. Consequently, the quality of evidence was moderate for the NIHSS, ADL, and ADR scores (Table 6).

4 Discussion

Stroke is the main cause of disability and the second leading cause of death in the world (Paul and Candelario-Jalil, 2021). Ischemic stroke has become a global health problem that

seriously threatens human life and health (Jiang et al., 2020). With the continuous development of medicine, the methods of treating ischemic stroke are also increasing, and TCM treatment has always played an important role in it. BYHWD is a classical Chinese medicine prescription for the treatment of ischemic stroke in the recovery period and has a good clinical effect on ischemic stroke in the recovery period (Liu et al., 2022). Therefore, this meta-analysis aimed to evaluate the clinical efficacy and safety of BYHWD in the recovery period of ischemic stroke patients.

A total of 39 studies involving 3,683 patients were included in this meta-analysis, and BYHWD combined with conventional treatment and conventional treatment alone were compared in



patients with ischemic stroke in the recovery period. Under normal circumstances, clinical ischemic stroke patients often leave symptoms of different degrees of neurological deficits. Improving the symptoms of this neurological deficit and improving the activities of daily living have always been the top priorities in the treatment of cerebral infarction (Xing and Bai, 2020). Therefore, in this study, the NIHSS was the primary outcome measure, and CSS, ADR, and ADL were the secondary outcomes. The above indicators were used as clinical trial observation and efficacy evaluation indicators. The National Institute of Health Stroke Scale (NIHSS) score (Yamal 2021), which is a quantitative indicator of the severity of the stroke, is often used as a surrogate endpoint in clinical research and stratifies patients according to the NIHSS score to guide clinical decision-making. Effective treatment was defined as a decrease in the NIHSS score by more than four points or complete disappearance of symptoms after treatment. The CSS score includes horizontal gaze, level of consciousness, speech, limb flexibility, and walking ability. The higher the score, the worse the patient's condition and the worse the neurological function (Cai and Zhang, 2022). The results of this study show that, compared with conventional treatment alone, BYHWD combined with conventional treatment can reduce the NIHSS score and CSS score of patients, suggesting that BYHWD can improve the neurological function of ischemic stroke patients in the recovery period. In terms of activities of daily living, the activities of daily living in the experimental group were stronger than those in the control group. Moreover, the results of the meta-analysis indicated that compared with the control group, the treatment of the experimental group in the recovery period of ischemic stroke did not increase the adverse reactions of patients. All the results prove that BYHWD is an effective therapy to improve the recovery period of ischemic

stroke, which is beneficial for relieving the patient's condition, promoting the improvement of the patient's neurological function, and improving the quality of life without increasing adverse reactions.

BYHWD comes from Wang Qingren's "Yilin Correction" in the Qing Dynasty. It is a commonly used prescription for the treatment of ischemic stroke. "This prescription treats hemiplegia, crooked eyes, slurred speech, salivation at the corners of the mouth, dry stools, frequent urination, and incontinence of enuresis" (Wu, 2019). This prescription has the compatibility characteristics of "not to remove blood stasis to activate blood, but to invigorate Qi to activate blood" (Liang et al., 2021). *Astragalus trimestris* L is the monarch drug in BYHWT, which has the effects of nourishing vitality, promoting blood circulation, and removing blood stasis; *Angelica sinensis* (Oliv.) Diels is the ministerial drug of the formula, which can activate blood and nourish blood and remove blood stasis; Other botanical drugs have activities of expectorating phlegm and dredging collaterals. The combination of the above drugs can have a synergistic effect and achieve the effects of nourishing Qi and promoting blood circulation, removing blood stasis, and dredging collaterals. As a popular traditional Chinese medicine formula, BYHWD was widely used for treating ischemic diseases. However, there are few studies focused on the effects of BYHWD on neurodegenerative diseases, and the underlying molecular mechanisms are largely elusive. Li Z *et al.* established a neurotoxic model in PC12 cells and adopted an innovative experimental grouping method to investigate the neuroprotective effects of BYHWD on neurotoxicity induced by 6-Hydroxydopamine (6-OHDA) exposure. They found that BYHWD had neuroprotective effects against the 6-OHDA-induced neurotoxicity *via* Akt/GSK3 β pathway based on serum pharmacology methodology. (Li et al., 2016). Another study found that BYHWD could modulate multiple signaling pathways including the Jak/Stat3/cyclin D1 signaling pathway, EGFR/PI3K/Akt/Bad/14-three to three signaling pathway, caveolin-1, and Hes1. The modulations of these cellular signaling pathways contributed to the anti-apoptotic cell death, improvement of the neural stem cell proliferation, astrogenesis, and neurogenesis in post-ischemia brains, subsequently inducing the recovery of the neurological functions in the post-ischemic brains (Chen X. et al., 2020). In addition, modern studies have shown that BYHWD can reduce cerebral infarct size and improve neurological deficits in ischemic stroke rats and attenuate neuronal damage in rats with cerebral ischemia/reperfusion (I/R) injury (Li et al., 2021); BYHWD can promote neurogenesis and angiogenesis in rats with cerebral ischemia (Zhuge et al., 2020); BYHWD can protect the integrity of the neurovascular unit and improve the permeability of the blood-brain barrier, thereby improving stroke caused by cerebral ischemia (Zheng et al., 2021). Therefore, BYHWD can effectively treat ischemic stroke and can be widely used in the clinical treatment of ischemic stroke.

TABLE 6 Evidence GRADE profile.

| Outcome (no. Of trials) | Quality assessment | | | | | Sequelae of stroke | | | Clinical efficacy and safety | Quality |
|-------------------------------|--------------------|---------------|--------------|-------------|---------------------|-----------------------|-------------------------------------|----------------|------------------------------------|---------|
| | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | BYHWD and CT | CT | 95% CI | Adverse reactions | |
| NIHSS Moderate | None ^b | No | No | No | None ^b | 1063/2121 (50.1%) | 1058/2121 (49.9%) | -1.75 to -1.12 | None | ⊕⊕⊕O |
| CSS Moderate | None ^b | No | No | No | None ^b | 294/568(51.8%) | 274/568(48.2%) | -2.02 to -0.34 | None | ⊕⊕⊕O |
| ADL Moderate | None ^b | No | No | No | None ^b | 1104/2194 (50.3%) | 1090/2194 (49.7%) 474/956(49.6%) | 3.06 to 5.61 | None | ⊕⊕⊕O |
| ADR Moderate | None ^b | No | No | No | None ^b | 482/956(50.4%) | | 0.88 to 1.61 | None | ⊕⊕⊕O |

NIHSS: national institute of health stroke scale; CSS: cincinnati stroke scale; ADL: activities of daily living; ADR: adverse drug reaction.

^aMost trials had an unclear risk of methodological bias. Evidence was therefore downgraded by one level.

^bPublication bias was not presented. The results were robust. Therefore, the evidence was not downgraded.

Limitations of this study: 1) Although the included trials were described as “random grouping”, most of the trials did not describe specific grouping methods, blinding, allocation concealment, *etc.*, so the possibility of selection bias cannot be ruled out; 2) Samples of most included studies were relatively small; 3) The efficacy evaluation of most studies was subject to a certain degree of subjectivity, and there was a lack of standard quantitative research; 4) Due to generally low quality of the included trials, this study can only draw very limited conclusions. There is an urgent need to improve the quality of the design and report of such studies.

5 Conclusion

Compared with conventional treatment alone, BYHWD combined with conventional treatment contributed to a significant improvement in clinical efficacy, neurological function, and activities of daily living, while it did not increase adverse reactions. Due to the limitations of this study, the quality of the included trials was generally low. In the future, more clinical trials with standardized designs, strict implementations, and large samples are needed to further verify the clinical efficacy and safety of BYHWD in the treatment of ischemic stroke in the recovery period and provide a more reliable evidence-based basis for clinical application.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

References

- Belova, A. N., Bogdanov, E. I., Zhadnov, V. A., Kamchatnov, P. R., and Kurushina, O. V. (2021). [Therapy of moderate cognitive impairment in the early recovery period of ischemic stroke]. *Zh. Nevrol. Psikiatr. Im. S. S. Korsakova* 121 (5), 33–39. doi:10.17116/jnevro202112105133
- Boulanger, J. M., Lindsay, M. P., Gubitz, G., Smith, E. E., Stotts, G., Foley, N., et al. (2018). Canadian stroke best practice recommendations for acute stroke management: Prehospital, emergency department, and acute inpatient stroke care, 6th edition, update 2018. *Int. J. Stroke* 13 (9), 949–984. doi:10.1177/1747493018786616
- Cai, G. X., and Liu, B. Y. (2010). Effect of ultra-micronized Buyang Huanwu decoction on neurological function, quality of life, and serum vascular endothelial growth factor in patients with cerebral infarction. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue* 22 (10), 591–594.
- Cai, Z., and Zhang, L. (2022). The effect of combined treatment with ginkgo diterpene lactone meglumine and ozagrel in patients with acute cerebral infarction and its influence on CSS score[J]. *Guizhou Med.* 46 (02), 251–252.
- Chalos, V., van der Ende, N. A. M., Mulder, M. J. H. L., Venema, E., and Dijkland, S. A. (2020). National Institutes of health stroke scale: An alternative primary outcome measure for trials of acute treatment for ischemic stroke. *Stroke* 51 (1), 282–290. doi:10.1161/STROKEAHA.119.026791
- Chen, H., Yao, X., Li, T., Lam, C. W. K., Zhang, R., Zhang, H., et al. (2020a). Compound kushen injection combined with platinum-based chemotherapy for stage III/IV non-small cell lung cancer: A meta-analysis of 37 RCTs following the PRISMA guidelines. *J. Cancer* 11 (7), 1883–1898. doi:10.7150/jca.40267

Author contributions

RW, JR, SL, XB, and WG are equal contributors and co-first authors.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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- Chen, X., Chen, H., He, Y., Fu, S., Liu, H., Wang, Q., et al. (2020b). Proteomics-guided study on Buyang huanwu decoction for its neuroprotective and neurogenic mechanisms for transient ischemic stroke: Involvements of EGFR/PI3K/Akt/Bad/14-3-3 and jak2/stat3/cyclin D1 signaling cascades. *Mol. Neurobiol.* 57 (10), 4305–4321. doi:10.1007/s12035-020-02016-y

- Chen, X., and Zhao, D. (2018). Analysis of the effect of Buyang Huanwu Decoction on 188 patients with cerebral infarction in convalescence. *Chin. Community Physician* 34 (26), 115117. doi:10.3969/j.issn.1007-614x.2018.26071

- Chen, Y., and Cao, J. (2016). Clinical observation on 35 cases of cerebral infarction in recovery period treated with combination of traditional Chinese and western medicine. *Pract. Integr. Chin. West. Med. Clin.* 16 (5), 16–18. doi:10.13638/j.issn.1671-4040

- Cumpston, M., Li, T., Chandler, J., Welch, V. A., and Higgins, J. P. (2019). Updated guidance for trusted systematic reviews: A new edition of the Cochrane Handbook for systematic reviews of interventions. *Cochrane Database Syst. Rev.* 10, ED000142. doi:10.1002/14651858.ED000142

- Diao, L. (2017). Study on clinical efficacy of Buyang Huanwu Decoction in treating 30 patients with cerebral infarction in convalescence. *China CME* 9 (18), 180–181. doi:10.3969/j.issn.1674-9308.2017.18.099

- Du, Q. (2018). Observation on the therapeutic effect of Buyang Huanwu Decoction on stroke recovery. *J. Chronic Dis.* 7, 1. doi:10.16440/j.cnki.1674-8166.20180517.001

- Egger, M., Davey Smith, G., Schneider, M., and Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ* 315, 629–634. doi:10.1136/bmj.315.7109.629

- Encephalopathy Emergency Collaborative Group of the State Administration of Traditional Chinese Medicine (1995). *Stroke diagnosis and efficacy evaluation criteria (trial version) [M]*. Beijing: China Traditional Chinese Medicine Press, 1–240.
- Fang, T., Wang, G., and Zhao, J. (2019). Effect of Buyang Huanwu Decoction on serum IGF-1 level and cognitive function of patients with cerebral infarction in convalescence. *Hainan Med. J.* 30 (23), 3027–3029. doi:10.3969/j.issn.1003-6350.2019.23.010
- Feske, S. K. (2021). Ischemic stroke. *Am. J. Med.* 134 (12), 1457–1464. doi:10.1016/j.amjmed.2021.07.027
- Guo, Q., Yang, S., Yang, D., Zhang, N., Li, X., Chen, T., et al. (2020). Differential mRNA expression combined with network pharmacology reveals network effects of Liangxue Tongyu Prescription for acute intracerebral hemorrhagic rats. *J. Ethnopharmacol.* 246, 112231. doi:10.1016/j.jep.2019.112231
- Guyatt, G. H., Oxman, A. D., Vist, G. E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., et al. (2008). Grade: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 336 (7650), 924–926. doi:10.1136/bmj.39489.470347.AD
- Han, S. (2014). Effect of Buyang Huanwu Decoction on the recovery of neurological function and daily living ability of patients with cerebral infarction in the recovery period (Qi deficiency and blood stasis syndrome). *Chin. J. Disabil. Med.* 11, 193–194. doi:10.13214/j.cnki.cjotadm.2014.11.184
- Ji, X. (2016). Clinical observation on the treatment of cerebral infarction of qi deficiency and blood stasis type with modified Buyang huanwu decoction. *Dis. Monit. Control* 10 (6), 458–459.
- Jiang, C. T., Wu, W. F., Deng, Y. H., and Ge, J. W. (2020). Modulators of microglia activation and polarization in ischemic stroke (Review). *Mol. Med. Rep.* 21 (5), 2006–2018. doi:10.3892/mmr.2020.11003
- Jiang, P. (2019). Quantitative evaluation and analysis of therapeutic effect of Buyang Huanwu Decoction on qi deficiency and blood stasis syndrome in stroke recovery. *Health Care Guide* 29, 252.
- Jin, C., Kwon, S., Cho, S. Y., Park, S. U., Jung, W. S., Moon, S. K., et al. (2021). A systematic review and meta-analysis of the effects of herbal medicine Buyang huanwu tang in patients with poststroke fatigue. *Evid. Based. Complement. Altern. Med.* 2021, 4835488. doi:10.1155/2021/4835488
- Jin, D., and Xu, Q. (2019). Study on the improvement of nerve function and quality of life of patients with cerebral infarction in the recovery period by Buyang Huanwu Decoction. *Electron. J. Clin. Med. Literature* 6 (A1), 174.
- Li, C., and Li, Z. (2010). The effect of supplementing qi and activating blood circulation on the quality of life and curative effect of patients with cerebral infarction in the recovery period. *J. Traditional Chin. Med.* 16 (6), 41–43. doi:10.3969/j.issn.1672-951X.2010.06.021
- Li, D. (2019). Prognostic analysis of patients with cerebral infarction in convalescence treated with Buyang Huanwu Decoction. *China Pract. Med.* 14 (13), 127–128. doi:10.14163/j.cnki.11-5547/r.2019.13.068
- Li, G. (2011). Clinical observation on modified Buyang huanwu decoction in treating cerebral infarction in recovery period[J]. *Med. Inf. late issue* 24 (1), 2. doi:10.3969/j.issn.1674-7860.2014.35.033
- Li, H., Peng, D., Zhang, S. J., Zhang, Y., Wang, Q., and Guan, L. (2021). Buyang Huanwu Decoction promotes neurogenesis via sirtuin 1/autophagy pathway in a cerebral ischemia model. *Mol. Med. Rep.* 24 (5), 791. doi:10.3892/mmr.2021.12431
- Li, R. (2014). Clinical observation on Buyang huanwu decoction in the treatment of cerebral infarction in the recovery period. *Inn. Mong. J. Traditional Chin. Med.* 33 (17), 10–11.
- Li, S., and Wei, Z. (2021). Effect of Buyang Huanwu Decoction on neurological function and serum oxLDL, MDA, SOD of stroke patients in recovery period. *Guangming Tradit. Chin. Med.* 36 (19), 3296–3298. doi:10.3969/j.issn.1003-8914.2021.19.032
- Li, T. (2018). Clinical observation of Buyang Huanwu decoction in treating cerebral infarction in convalescence. *Food Ther. Health Care* 1, 267.
- Li, X. (2012). Analysis of the clinical efficacy of Buyang Huanwu Decoction in the recovery period of cerebral infarction. *China Med. Eng.* 20 (12), 125.
- Li, Z., Wang, H., Wang, Q., and Sun, J. (2016). Buyang huanwu decoction vigorously rescues PC12 cells against 6-OHDA-induced neurotoxicity via akt/gsk3 β pathway based on serum pharmacology methodology. *Rejuvenation Res.* 19 (6), 467–477. doi:10.1089/rej.2015.1798
- Liang, R., Tang, Q., Wang, L., Yue, P., and Zhu, L. (2021). Buyang huanwu decoction combined with probiotics or prebiotics for functional recovery from stroke: A meta-analysis protocol for systematic review. *Med. Baltim.* 100 (51), e28371. doi:10.1097/MD.00000000000028371
- Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gotzsche, P. C., Ioannidis, J. P. A., et al. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ* 339, b2700. doi:10.1136/bmj.b2700
- Lin, X. (2014). Buyang Huanwu Decoction in the treatment of 41 patients with cerebral infarction in the recovery period. *Modern Distance Education of Chinese Med.* 12 (11), 129–130. doi:10.3969/j.issn.1672-2779.2014.11.082
- Liu, D. (2018). Clinical observation on Buyang huanwu decoction in treating patients with qi deficiency and blood stasis syndrome in the recovery period of cerebral infarction. *Electron. J. Cardiovasc. Dis. Integr. Traditional Chin. West. Med.* 6 (15), 143.
- Liu, E. H., Qi, L. W., Cheng, X. L., Peng, Y. B., and Li, P. (2010). Simultaneous determination of twelve bioactive constituents in Buyang Huanwu decoction by HPLC-DAD-ELSD and HPLC-TOF/MS. *Biomed. Chromatogr.* 24 (2), 125–131. doi:10.1002/bmc.1269
- Liu, M., Pu, Y., Gu, J., He, Q., Liu, Y., Zeng, Y., et al. (2021). Evaluation of zhihong huoxue tongyu capsule in the treatment of acute cerebral infarction: A systematic review and meta-analysis of randomized controlled trials. *Phytomedicine.* 86, 153566. doi:10.1016/j.phymed.2021.153566
- Liu, W., Zhang, Y., Zhou, X., and Zeng, K. (2022). Research progress on the mechanism of Buyang Huanwu Decoction against cerebral ischemia[J]. *New Chin. Med. Clin. Pharmacol.* 33 (03), 411–418.
- Meng, W., Li, J., and Zhang, L. (2014). Clinical observation on modified Buyang huanwu decoction in the treatment of cerebral infarction recovery (qi deficiency and blood stasis syndrome). *J. Yunnan Univ. Traditional Chin. Med.* 2, 74–76.
- Paul, S., and Candelario-Jalil, E. (2021). Emerging neuroprotective strategies for the treatment of ischemic stroke: An overview of clinical and preclinical studies. *Exp. Neurol.* 335, 113518. doi:10.1016/j.expneurol.2020.113518
- Shang, H. (2021). Effect of Buyang huanwu decoction on cerebral infarction recovery. *Big Vis. Health* 9, 85.
- Shao, L., She, Y., Yong, S., Chen, B., Yi, J., Li, Y., et al. (2022). An evidence-based evaluation of Buyang huanwu decoction for the treatment of the sequelae of stroke: A PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. *Phytomedicine.* 104, 154312. doi:10.1016/j.phymed.2022.154312
- Shi, W. (2016). Observation on the clinical efficacy of traditional Chinese medicine in treating patients with stroke in convalescence. *Health Care Guide* 32, 23.
- Stinear, C. M., Lang, C. E., Zeiler, S., and Byblow, W. D. (2020). Advances and challenges in stroke rehabilitation. *Lancet. Neurol.* 19 (4), 348–360. doi:10.1016/S1474-4422(19)30415-6
- Strini, V., Piazzetta, N., Gallo, A., and Schiavolin, R. (2020). Barthel index: Creation and validation of two cut-offs using the BRASS index. *Acta Biomed.* 91 (2-S), 19–26. doi:10.23750/abm.v91i2-S.9226
- Sui, W. (2014). Li aiping clinical study on Buyang huanwu decoction to improve neurological function defects in the recovery period of ischemic stroke. *New Chin. Med.* 46 (7), 40–42. doi:10.13457/j.cnki.jncm.2014.07.19
- Tao, Z. (2009). Reliability, validity and sensitivity of Chinese scale for clinical neurological deficit of stroke patients. *Acad. J. Sec. Mil. Med. Univ.* 30 (03), 283–285. doi:10.3724/sp.j.1008.2009.00283
- The Fourth National Academic Conference on cerebrovascular disease (1996). sScoring criteria for clinical neurological deficits of stroke patients [J]. *Chin. J. Neurology* 29 (6), 381–382.
- Wang, H., Ma, Z., and Shi, Z. (2012). Observation on the therapeutic effect of Buyang Huanwu Decoction on 54 cases of cerebral infarction in the recovery period. *Yunnan J. Traditional Chin. Med.* 6 (6), 47–48. doi:10.3969/j.issn.1007-2349.2012.06.027
- Wang, K., Lei, L., Qiao, Y., Liang, R., and Duan, J. (2021). Network pharmacology-based prediction of the active compounds and mechanism of Buyang Huanwu Decoction for ischemic stroke. *Exp. Ther. Med.* 22 (4), 1050. doi:10.3892/etm.2021.10484
- Wang, Q. (1999). *Yilin correction*. Tianjin Science and Technology Press, 32.
- Wang, X., Liu, Z., Sui, X., Wu, Q., Wang, J., and Xu, C. (2019). Elemene injection as adjunctive treatment to platinum-based chemotherapy in patients with stage III/IV non-small cell lung cancer: A meta-analysis following the PRISMA guidelines. *Phytomedicine* 59, 152787. doi:10.1016/j.phymed.2018.12.010
- Wang, X., Wang, Y., Liu, Z., and Qu, L. (1999). A comparative study on the reliability and validity of four stroke scales. *Chin. J. Phys. Med. Rehabilitation* 3, 13–16.
- Wang, X., Wang, R., and Xie, C. (2021). The clinical effect of Buyang Huanwu Decoction on stroke of qi deficiency and blood stasis in convalescence. *J. Clin. Ration. Drug Use* 14 (26), 51–53. doi:10.15887/j.cnki.13-1389/r.2021.26.018
- Wu, J. (2007). Study on reliability and validity of four stroke scales. Master's Electronic Journal. Tianjin (China): Tianjin Medical University.

- Wu, J. (2021). Analysis of the clinical effect of Buyang Huanwu Decoction on patients with qi deficiency and blood stasis syndrome in the recovery period of cerebral infarction. *Zhonghua Health Care* 39 (17), 17–18.
- Wu, Q., Yao, X., Chen, H., Liu, Z., Li, T., Fan, X., et al. (2020). Long-term aspirin use for primary cancer prevention: An updated systematic review and subgroup meta-analysis of 29 randomized clinical trials. *J. Cancer* 11 (21), 6460–6473. doi:10.7150/jca.49001
- Wu, W. (2019). Study on the mechanism of Buyang Huanwu Decoction in the treatment of ischemic stroke [J]. *Electron. J. Clin. Med. Literature* 6 (17), 193. doi:10.21203/rs.3.rs-24632/v1
- Xiang, J. (2019). Clinical observation on the treatment of cerebral infarction in the recovery period with modified Buyang huanwu decoction. *Guangming Tradit. Chin. Med.* 34 (20), 3149–3150. doi:10.3969/j.issn.1003-8914.2019.20.034
- Xing, Y., and Bai, Y. (2020). A review of exercise-induced neuroplasticity in ischemic stroke: Pathology and mechanisms. *Mol. Neurobiol.* 57 (10), 4218–4231. doi:10.1007/s12035-020-02021-1
- Xu, H., Zou, Y., Zhou, H., and Lv, J. (2017). Evaluation of therapeutic effect of Buyang Huanwu Decoction on patients with ischemic stroke in the recovery period. *World J. Integr. Traditional West. Med.* 12 (08), 1155–1157+1176. doi:10.13935/j.cnki.sjzx.170832
- Xu, G. (2014). Observation on the therapeutic effect of Buyang Huanwu Decoction on 60 cases of cerebral infarction in the recovery period. *Med. Inf.* 37, 426. doi:10.3969/j.issn.1006-1959.2014.37.668
- Xue, L., and Xue, J. (2015). Clinical observation on 36 cases of cerebral infarction in recovery period treated with Buyang huanwu decoction. *Pharmacol. Clin. Med. Traditional Chin. Med.* 31 (2), 179–180.
- Yamal, J. M. (2021). National Institutes of health stroke scale as an outcome measure for acute stroke trials. *Stroke* 52 (1), 142–143. doi:10.1161/STROKEAHA.120.032994
- Yang, J., Wen, Y., and Zhou, H. (2021). Clinical observation of Buyang Huanwu Decoction in the treatment of cerebral infarction in convalescence. *J. Pract. Chin. Med.* 37 (12), 2034–2035.
- Yang, S. (2020). Observation on the therapeutic effect of Buyang Huanwu Decoction on the syndrome of qi deficiency and blood stasis in the recovery period of ischemic stroke. *Electron. J. Cardiovasc. Dis. Integr. Traditional Chin. West. Med.* 8 (24), 164167.
- Yang, Y. (2018). Observation on the application of Buyang Huanwu Decoction in the recovery period of stroke. *Diet health care* 5 (41), 114–115. doi:10.3969/j.issn.2095-8439.2018.41.138
- Yang, Z. (2022). Based on the "brain-gut axis" to explore the research progress of traditional Chinese medicine in the treatment of ischemic stroke [J]. *J. Liaoning Univ. Traditional Chin. Med.* 24 (04), 130–134.
- Yu, F. (2013). Analysis of clinical efficacy of Buyang Huanwu Decoction in treating cerebral infarction in convalescence. *Chin. Med. Guide* 22, 263–264.
- Zhang, G., and Xiong, C. (2020). Observation on the effect of integrated traditional Chinese and Western medicine in treating sequelae of cerebral apoplexy of qi deficiency and blood stasis type and analysis on the influence of neurological recovery. *Health Compuls.* 11, 165.
- Zhang, J. (2018). The improvement effect of Buyang Huanwu Decoction on the depressive state of patients with stroke in the recovery period. *China Higher Medical Education*, 134. 10.3969/j.issn.1002-1701.2018.10.070.
- Zhang, L. (2013). Effect of buyang huanwu decoction on neurological function and quality of life of patients with cerebral infarction in recovery period. *China Pharmaceutical.* 22, 106. 10.3969/j.issn.1006-4931.2013.20.059.
- Zhang, M. (2017). 50 cases of cerebral infarction of qi deficiency and blood stasis type in convalescence were treated with integrated traditional Chinese and Western medicine. *Chin. Folk. Med.* 26 (23), 111–112119.
- Zheng, J. (2016). Observation on the therapeutic effect of Buyang Huanwu Decoction in the recovery period of cerebral infarction. *Electron. J. Clin. Med. Literature* 3 (28), 5590–55905592.
- Zhao, X., and Zhou, M. (2021). Research progress of traditional Chinese medicine in the treatment of ischemic stroke[J]. *Med. Rev.* 27 (22), 4548–4552.
- Zheng, X. Y., Zhang, Y. H., Song, W. T., Cao, H., and Liu, J. X. (2021). Effects of Buyang huanwu decoction on neurovascular units after cerebral ischemia: A review. *Zhongguo Zhong Yao Za Zhi* 46 (20), 5226–5232. doi:10.19540/j.cnki.cjcm.20210610.706
- Zhuge, L., Fang, Y., Jin, H., Li, L., Yang, Y., Hu, X., et al. (2020). Chinese medicine Buyang Huanwu decoction promotes neurogenesis and angiogenesis in ischemic stroke rats by upregulating miR-199a-5p expression. *Zhejiang Da Xue Xue Bao Yi Xue Ban.* 49 (6), 687–696. doi:10.3785/j.issn.1008-9292.2020.12.03
- Zuo, Q., and Jin, L. (2020). Observation on therapeutic effect of Buyang Huanwu Decoction combined with Western medicine in the recovery period of cerebral infarction. *Grassroots Med. Forum* 24 (13), 1890–1892. doi:10.19435/j.1672-1721.2020.13.071