META-ANALYSIS

# Meta-Analysis of the Effect of Conventional Western Medicine Therapy Supplemented with Buyanghuanwu Decoction on Neurological Function and Condition Improvement of Patients with Cerebral Apoplexy in Convalescence

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## ABSTRACT

Meta-analysis was used to analyze the efficacy of conventional western medicine plus Buyanghuanwu Decoction in the treatment of convalescent patients with stroke, and to observe its influence on the neurological function and condition of patients. According to the research direction and set keywords, the research literature was retrieved from Wanfang Medical Science, CNKI, VIP, PubMed and other domestic and foreign literature databases. A total of 13 articles with 1023 patients were included in this meta-analysis, with a large sample size. Outcome measures of the meta-analysis included efficacy, National Institutes of Health Stroke Scale (NIHSS) score, Barthel Index Rating Scale (BI) score, C-reactive protein (CRP) and homocysteine (Hcy) score. Compared with western medicine group, the increase of BI score and the decrease of NIHSS score, CRP and Hcy in combined medicine group were greater (P<0.05). Conventional Western medicine combined with Buyang Huanwu Decoction can improve the rehabilitation effect, living ability and neurological function of patients with stroke, and reducing the inflammatory response, it is beneficial to create favorable conditions for patients' rehabilitation and improve prognosis, which is worthy of clinical application. The effect of this protocol on long-term survival of patients can be further analyzed in the future. (*Altern Ther Health Med.* 2024;30(7):72-77).

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## INTRODUCTION

Stroke is a common cerebrovascular disease in clinical practice. The main types are ischemic stroke and hemorrhagic stroke. Ischemic strokes are usually caused by vertebral artery stenosis, thrombosis, and spasms of cerebral arteries, while hemorrhagic strokes are mainly caused by high blood pressure and cerebral atherosclerosis. Ischemic stroke is the main type of stroke, accounting for more than 80.00%, with high disability rate and fatality rate, posing a serious threat to patients' health and life safety.[1]

Clinical data show that the incidence of sequelae in stroke patients can reach 70% or more than 80%, of which motor dysfunction is the most common, accounting for 70% to 80% of sequelae, cognitive dysfunction and limb sensory loss account for 20% to 30%, leading to poor rehabilitation effect and reduced quality of life.[2] At the present stage, aspirin, edaravone and other western drugs are commonly used in the treatment of patients with clinical stroke. Although certain results can be achieved, the treatment effect of some patients still fails to meet expectations, which is unfavorable to the improvement of the prognosis of patients.[3]

According to Traditional Chinese medicine, stroke belongs to the category of "stroke" and should be treated with "wind-dispelling phlegm, activating blood circulation and dredging collaterals", Among them, the Buyanghuanwu Decoction has the efficacy of tonifying qi, activating blood and clearing collaterals, which is the main treatment for the evidence of qi deficiency and blood stasis in stroke and is widely used in the sequelae of cerebrovascular accidents, and its efficacy has been certified by the majority of experts.[4] The purpose of this study was to evaluate the efficacy of Buyanghuanwu Decoction as a conventional western medicine supplement in the treatment of stroke patients.

## METHODS

### Literature Retrieval

The relevant literatures of controlled clinical trials were retrieved from domestic and foreign libraries. The research direction is to improve the effect of conventional Western medicine therapy combined with Buyang Huanwu Decoction on the neurological function and condition of convalescent stroke patients. The literature search period was from January 2013 to May 2022. Search for single or combined keywords in various libraries, Including efficacy, National Institutes of Health Stroke Scale (NIHSS) score, Barthel index, BI, C-reactive protein (CRP), homocysteine (Hcy), efficacy, National Institutes of Health Stroke Scale (NIHSS) score, Barthel Index (BI) score, C-reactive protein (CRP), homocysteine amino acid (Hcy). By random grouping method, the two treatment schemes of Western medicine alone and Western medicine combined buyang Huanwu Decoction were compared respectively. This study was approved by relevant medical institutions, and the rate of missing persons at follow-up was &lt. 20%, high data integrity, including a series of operations set in this study efficacy, NIHSS score, BI score, CRP, Hcy observation indicators of any one or more clinical laboratory indicators detection, no obvious errors. Literature with poor logic difference and serious repetition should be excluded. Clinical trials with obvious errors, incomplete data, unable to complete the literature should be excluded; Literature on basic experiments in cells and animals needs to be excluded; References inconsistent with the research direction of this study were excluded.

### Outcome measures

NIHSS score and BI score can reflect the neurological function and activity of patients, while CRP and Hcy can reflect inflammation and reflect the treatment effect and rehabilitation of patients, thus the observational indicators of this study included efficacy, NIHSS score, BI score, CRP and Hcy.

### Literature quality evaluation

The Jadad scale includes four items: generation of random sequence, randomization hiding, blind method, withdrawal and withdrawal, which can effectively reflect the quality of literature. The total score of the modified Jadad scale was 1-7, and this scale evaluated the literature quality. If ≤ 3, the literature was classified as low quality, and if >3, the literature was classified as high quality.

### Statistical analysis

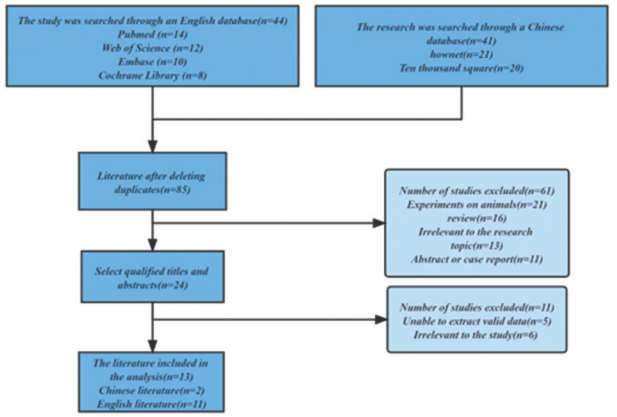
RevMan5.2 statistical software was used for analysis. *RR* is used to represent count data, relative risk, SMD is used to represent analysis statistics, and standardized mean difference, and 95% *CI* was used as the representation of effect size. Chi-square test was used to test the heterogeneity among the experiments. If the heterogeneity was small ($P > .05$, $I^2 \leq 50\%$), the fixed effect model was used to analyze. If the inter-group heterogeneity was large ($P < .05$, $I^2 > 50\%$), subgroup analysis was performed, and if there was no obvious clinical cause, random effects model was used for analysis. Funnel plot and Egger test were used for publication bias, and $P < .05$ was considered statistically significant.

**Table 1.** Literature inclusion information and quality

| the first author | The year of publication | sample capacity | Outcome indicators | Quality of literature |
|---|---|---|---|---|
| Chen AL[5] | 2018 | 100/100 | ①②③ | 4 |
| Chen WQ[6] | 2021 | 46/46 | ①②③ | 4 |
| Cui H[7] | 2016 | 36/36 | ② | 2 |
| DiMQ[8] | 2019 | 40/40 | ①②④ | 4 |
| Huang HS[9] | 2022 | 50/50 | ①②③④⑤ | 6 |
| Ji YY[10] | 2017 | 55/55 | ①②③⑤ | 5 |
| Li HS[11] | 2016 | 42/42 | ①② | 3 |
| Wang Y[12] | 2019 | 50/50 | ①②③④⑤ | 6 |
| XuAX[13] | 2017 | 30/30 | ①②③④⑤ | 6 |
| Xu H[14] | 2017 | 85/85 | ①② | 3 |
| Zhang D[15] | 2013 | 60/60 | ② | 2 |
| Zhang JP [16] | 2017 | 80/80 | ①② | 3 |
| Zhong FF[17] | 2021 | 360/360 | ①② | 4 |

Note: ① efficacy; ② NIHSS score; ③ BI score; ④ CRP; ⑤ Hcy.

**Figure 1.** Flow chart of literature screening




## RESULTS

### Retrieval results and features

A total of 13 literatures matching the research direction and keywords were screened out after searching the Chinese and English database, including 2 English and 11 Chinese literatures, 5 low-quality literatures and 8 high-quality literatures. Attached are Table 1[5-17] and Figure 1 are literature quality.

### Literature bias

A total of 11 Chinese and 2 English literatures were included, and no significant publication bias was found. Attached Figures 2-3.

### Meta-analysis of efficacy differences

A total of 11 efficacy related literatures were included, with significant heterogeneity among literatures ($I^2 = 7.0\%$, $P = .37$). Random effects model analysis showed that the combination group had higher efficacy and statistically significant differences [$P < .00001$]. It is suggested that the combined use of Buyanghuanwu Decoction can improve the curative effect on stroke patients. As shown in figure 4-5.

**Figure 2.** Overall literature bias

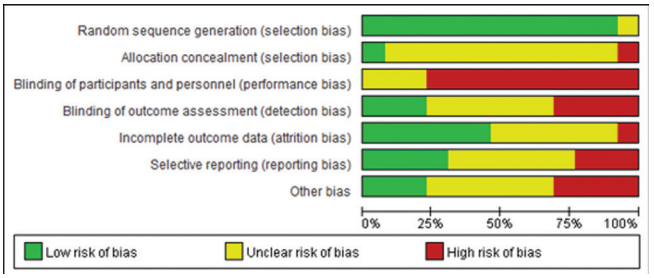
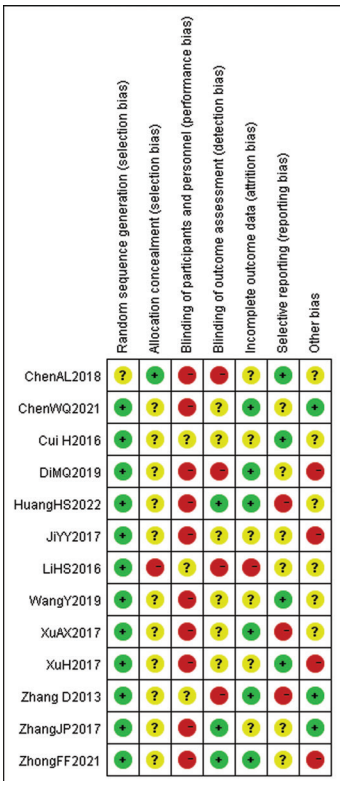



**Figure 3.** Bias of single literature




**Meta-analysis of differences in neurological function scores**

A total of 13 literatures related to NIHSS scores were included, with significant heterogeneity among all literatures ($I^2$ = 97.0%, $P$ < .00001). The reason of high heterogeneity may be related to subjective factors. Random effects model analysis showed that the combined group had lower NIHSS scores and statistically significant differences [$P$ < .00001]. These results suggest that the combined use of Buyanghuanwu Decoction can reduce NIHSS score of stroke patients. As shown in figure 6 and 7.

**Meta-analysis of differences in living ability scores**

A total of 6 BI score-related literatures were included, with significant heterogeneity among them ($I^2$ = 60.0%, $P$ = .03). The reason of high heterogeneity may be related to subjective factors. Random effect model analysis showed that the combined group had higher BI scores and statistically significant differences [$P$ < .00001]. It is suggested that the combined application of Buyanghuanwu Decoction can increase the BI score of stroke patients. As shown in figure 8-9.

**Figure 4.** Forest map of efficacy meta-analysis

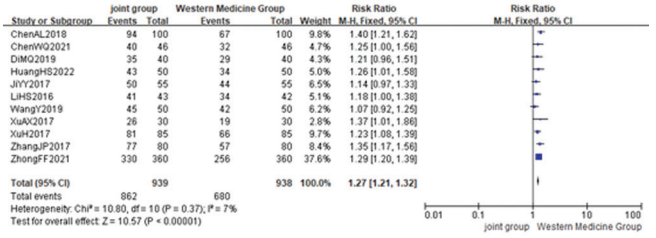



**Figure 5.** Funnel plot of efficacy meta-analysis

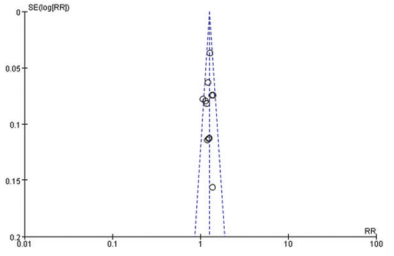



**Figure 6.** NIHSS score meta-analysis of forest map.

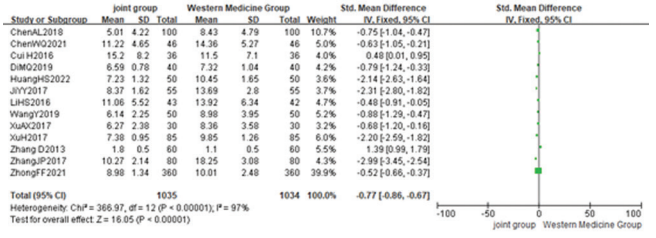



**Figure 7.** Funnel plot of NIHSS score meta-analysis

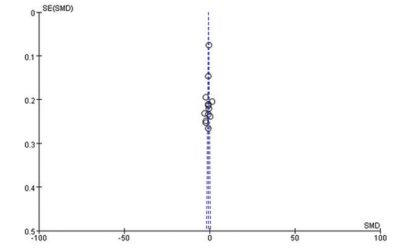



**Figure 8.** BI score meta-analysis of forest map

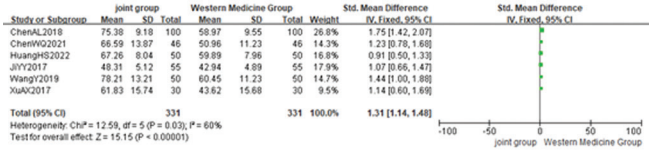



**Figure 9.** Funnel plot of BI score meta-analysis

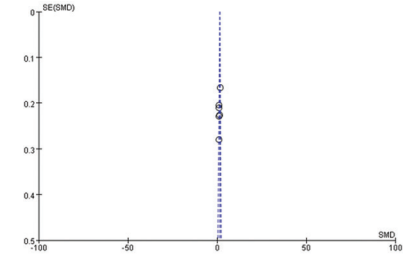


**Figure 10.** Forest map of CRP difference meta-analysis

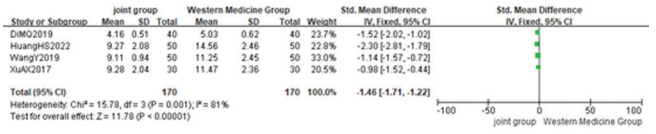



**Figure 11.** Funnel plot of CRP difference meta-analysis

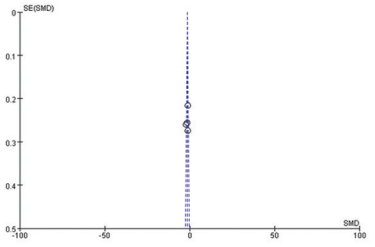



**Figure 12.** Hcy difference meta-analysis forest map

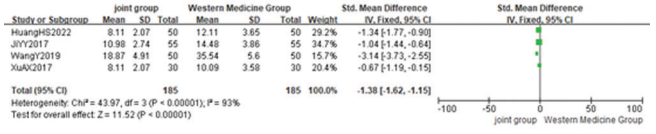
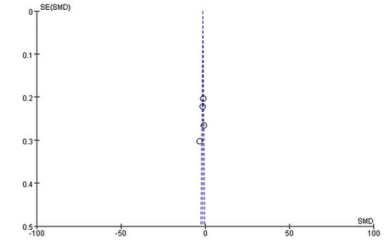



**Figure 13.** Funnel plot of Hcy difference meta-analysis




**Meta-analysis of differences in CRP and Hcy levels**

**Meta-analysis of CRP differences**

A total of 4 crP-related literature were included, with significant heterogeneity among them ($I^2$ = 81.0%, $P$ = .001). A total of 4 Hcy-related literatures were included, with significant heterogeneity among them ($I^2$ = 93.0%, $P$ < .00001). The heterogeneity of CRP and Hcy levels may be related to the different detection methods and detection time. Random-effects model analysis showed that CRP levels were statistically lower in the combined group [$P$ < .00001]. It is suggested that the combined application of Buyanghuanwu Decoction can reduce CRP level in stroke patients. As shown in figure 10 to 11. Random effect model analysis showed that the combined group had lower Hcy levels and statistically significant differences [$P$ < .00001]. These results suggest that the combined use of Buyanghuanwu Decoction can reduce the level of Hcy in stroke patients. As shown in figure 12-13.

## DISCUSSION

Emotional ups and downs fluctuate greatly, then it is easy to stimulate the human brain nerves, resulting in the blood can not be smoothly transmitted to the brain, excessive intake of alcohol and tobacco will lead to blood system disorders, triggering insufficient blood supply to the brain. Stroke causes blood circulation disorders under the synergistic action of multiple factors, which leads to local tissue ischemia and hypoxia, and ultimately leads to tissue necrosis. Limb numbness, dyskinesia and paralysis are the main clinical manifestations, which have a serious impact on patients' quality of life.[18] At present, thrombolytic therapy is the first clinical treatment, which can effectively dredge patients' blocked blood vessels and improve patients' prognosis, thus reducing the risk of disability and death. However, thrombolytic therapy has very strict clinical conditions and relatively high treatment cost and has relatively low acceptance among clinical patients. Therefore, clinical anticoagulant therapy and defibration therapy are the main treatment options. Although conventional Western drugs can relieve the clinical symptoms of patients, the disease is prone to recurrence and has no significant improvement effect on brain tissue damage.[19] Of traditional Chinese medicine theory is that the pathogenesis of stroke is not qi and blood, imbalance of Yin and Yang, qi and blood is less impact on the brain and is closely linked with the disorder of viscera, qi and blood can cause the body functioning, resulting in movement disorders with severe symptoms such as hemiplegia, eye mouth askew, against the patient's follow-up, clinical should with calm autumn zephyrlily, eliminating phlegm and blood stasis as the therapeutic principles, It can help to improve the neurological function of patients, and then promote the improvement and recovery of clinical symptoms.[20]

Buyanghuanwu soup is a clinically common prescription of traditional Chinese medicine treatment of stroke. In the body functioning of qi and blood in the veins, deficiency of qi and blood stasis resistance induced by both has good efficacy, side effect of huangqi can play to fill gas T2DM, party of angelica has a remarkable achievement for activating blood circulation and the sichuan dome, red paeony root, safflower, peach kernel, etc for medicinal herbs can also play a stasis T2DM, supplement the analgesic efficacy, Digilong plays the role of channeling meridians and activating collaterals and circulates all over the body. The prescription of Chinese herbal medicines takes both qi and blood as well as samples, and the combination of many medicines can play the role of supplementing qi and activating blood in a total way.[21,22] This study results show that the combined use of tonifying Yang also five decoction can obviously improve the clinical curative effect and life ability score, at the same time, effectively reduce the NIHSS score, prompt repair Yang also five soup with conventional western medicine therapy can relieve nerve function damage in patients with cerebral apoplexy, promote the recovery of neural function in patients with, and effectively improve the curative effect of patients with life ability, It is consistent with previous research literature. Analysis of the reasons are as follows: The reuse of Astragalus membranaceus in Buyanghuanwu Decoction stimulates the excitation conduction of the nervous system, helps to improve the symptoms of cerebral edema in patients with stroke, promotes brain recovery and reduces the infarct

area, and plays a role in promoting the recovery of neurological function from many aspects. Ultimately also, five decoction has a good effect of tonifying qi, T2DM, can improve brain blood circulation and blood supply obstacles, promote brain function recovery, at the same time can reduce the vascular tension by adjusting the brain blood flow dynamics, thus improving the elasticity of the blood vessels and lesions of hypoxia ischemia state, promote patients with nerve functional recovery, and at the same time improve the ability of daily life and enhance the curative effect.[23]

Hcy is the body of a sulfur-containing amino acid metabolites, Hcy levels rising exception will stimulate excessive oxygen free radical generation, leading to lipid peroxidation aggravating, causing oxidative stress response, at the same time, could induce a large number of platelet aggregation, adhesion, and thus promote thrombosis, and CRP can reflect the state of the body's inflammatory response to a sensitive indicators, Elevated CRP level indicates severe inflammatory response in patients, which in turn has a serious impact on the efficacy and prognosis of patients.[24] In this study, Hcy and CRP decreased more significantly in the combined group, suggesting that conventional Western medicine treatment combined with Buyanghuanwu Decoction can significantly inhibit the inflammatory response and thrombosis process of the body, thus delaying the disease progression of patients. It is speculated that the main reason may be the reuse of Astragalus membranaceus in Buyanghuanwu Decoction. The active ingredient of astragalus membranaceus glucoside has bactericidal and anti-inflammatory effects, which can effectively inhibit the secretion level of inflammatory factor CRP in patients, thus reducing inflammatory reactions. In addition, the radix paeoniae paeoniae in the prescription contains more active components of total glucosides of radix paeoniae. This ingredient can play a positive role in anticoagulation, antithrombotic and anti-platelet aggregation, thus effectively inhibiting the secretion and production of Hcy.[25]

Whole literature still exists on the design idea of this study, including the number of less, lack of support, and outcome indicators in English literature are not congruent; the above three deficiencies may lead to research data and bias issues, this study use during stroke rehabilitation in patients with routine western medicine joint repair Yang also five soup treatment as the breakthrough point, In the follow-up study, hemodynamics related indicators can be added for systematic analysis, and research design ideas can be further improved and validated based on the expansion of the number of sample literatures.

However, the study is observational, and the results can only reflect that the improvement of treatment after Buyang Huanwu decoction is related to the decrease of inflammatory response, but a causal relationship cannot be established. It is necessary to further analyze the causal relationship between the enhancement of treatment effect and the changes of CRP and Hcy. A limitation of this study is that there is high heterogeneity, which may have influenced the results, and there may be unmeasured confounding variables. More confounding variables need to be included in the future to improve the scientific nature of the study.

In summary, during the rehabilitation period of stroke patients, the combination of conventional Western medicine supplementation-yang Wutang therapy can improve clinical treatment effect and life ability, help to improve the neurological function of patients, inhibit the abnormal secretion of inflammatory factors, inhibit the inflammatory response of patients, and promote the rehabilitation of stroke patients from various aspects. It also has potential benefits in reducing the sequelae of patients, improving the quality of life and improving the long-term prognosis, which is worthy of clinical promotion and application.

## ETHICAL COMPLIANCE

Not applicable.

## CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

## AUTHOR CONTRIBUTIONS

RL, XZ and BF designed the study and performed the experiments, LM and QM collected the data, LM, QM and YY analyzed the data, RL, XZ and BF prepared the manuscript. All authors read and approved the final manuscript. RL and XZ contributed equally to this work.

## FUNDING

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