Check for updates

OPEN ACCESS

EDITED BY Viola B. Morris, Emory University, United States

REVIEWED BY Mina Bagheri Varzaneh, University of Illinois Chicago, United States Yongsheng Chen, Jinan University, China

*CORRESPONDENCE Lechang Zhan, ⋈ zlc6612@163.com

RECEIVED 15 April 2024 ACCEPTED 07 October 2024 PUBLISHED 22 October 2024

CITATION

Zhan J, Xu X, Zhu Y, Liu L, Chen H and Zhan L (2024) Shuxuening injection for treating acute ischemic stroke: a PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. *Front. Pharmacol.* 15:1407669. doi: 10.3389/fphar.2024.1407669

COPYRIGHT

© 2024 Zhan, Xu, Zhu, Liu, Chen and Zhan. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Shuxuening injection for treating acute ischemic stroke: a PRISMA-compliant systematic review and meta-analysis of randomized controlled trials

Jie Zhan^{1,2}, Xiaowen Xu³, Yanzhen Zhu², Lin Liu³, Hongxia Chen^{1,3,2} and Lechang Zhan^{1,2}*

¹Department of Rehabilitation, Guangdong Provincial Hospital of Chinese Medicine, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China, ²The Second Clinical College of Guangzhou University of Chinese Medicine, Guangzhou, China, ³Medical College of Acu-Moxi and Rehabilitation, Guangzhou University of Chinese Medicine, Guangzhou, China

Background: Using Shuxuening injection (SXNI) for acute ischemic stroke (AIS) is popular in China, but its efficacy and safety remain controversial.

Purpose: This study aims to assess the efficacy and safety of SXNI as an add-on therapy for AIS.

Study design: Systematic review and meta-analysis.

Methods: We searched for randomized controlled trials (RCTs) on SXNI for AIS in seven databases and two clinical trial registration platforms from their inception to January 2023. We used the Cochrane risk of bias tool to assess the methodological quality of the included studies and performed the metaanalysis with R software. The primary outcome was clinical efficacy, assessed by the clinical effective rate (CER). The secondary outcomes were neurological function, activities of daily living (ADL), and adverse events (AEs).

Results: In total, 116 studies with 12,401 participants were included in this review. Fifteen (12.9%) studies were judged to be of moderate to high quality. SXNI plus conventional treatments (CTs) improved the CER compared with CTs alone (risk ratio [RR]: 1.21, 95% confidence interval [CI]: 1.17–1.25, p < 0.0001) or CTs plus other injections (RR: 1.18, 95% CI: 1.15–1.21, p < 0.0001). SXNI plus CTs reduced the National Institute of Health Stroke Scale score compared with CTs alone (mean difference [MD]: -4.00, 95% CI: -5.22 to -2.78, p < 0.0001) or CTs plus other injections (MD: -2.28, 95% CI: -3.41 to -1.16, p < 0.0001). SXNI plus CTs alone (MD: -2.00 decreased the CTs alone (MD: -0.001) compared with CTs alone (MD: -0.001) compared with CTs alone (MD: -0.001) compared the CTS alone (MD: -0.001) comp

Abbreviations: ADL, activities of daily living; AEs, adverse events; AIS, acute ischemic stroke; BI, Barthel index; CBM, Chinese biological medicine database; CI, confidence interval; CER, clinical effective rate; CNKI, China national knowledge infrastructure; CONSORT, consolidated standards of reporting trials; CSS, Chinese Stroke Scale; CT, computed tomography; CTs, conventional treatments; EVT, endovascular thrombectomy; GBE, Ginkgo biloba extract; GRADE, Grading of Recommendation, Assessment, Development, and Evaluation; IVT, intravenous thrombolysis; MRI, magnetic resonance imaging; CND, clinical neurological deficit; NIHSS, National Institutes of Health Stroke Scale; RCTs, randomized controlled trials; ROB, risk of bias; RR, risk ratio; SMD, standardized mean difference; SXNI, shuxuening injection; PAF, platelet-activating factor; PRISMA, preferred reporting items for systematic reviews and meta-analysis; VIP, Chinese scientific journal database; WMD, weighted mean difference.

-5.01, 95% CI: -7.38 to -2.65, p < 0.0001) or CTs plus other injections (MD: -4.31, 95% CI: -5.75 to -2.88, p < 0.0001). SXNI plus CTs was superior for increasing the Barthel index score compared with CTs alone (MD: 11.58, 95% CI: 8.27–14.90, p < 0.0001) or CTs plus other injections (MD: 5.43, 95% CI: 0.48–10.39, p = 0.0317). The level of evidence for each outcome was assessed as low to very low. The most common AEs of SXNI were cardiovascular system events, and all these AEs were mild.

Conclusion: SXNI combined with CTs maybe better than CTs alone or CTs plus other injections for improving the clinical efficacy, neurological function, and ADL of AIS patients, with relatively reliable safety. However, due to the low quality of the included studies, more rigorously designed RCTs with large sample sizes should be conducted in the future.

Systematic Review Registration: www.crd.york.ac.uk, identifier (CRD42023418565).

KEYWORDS

shuxuening injection, acute ischemic stroke, traditional Chinese medicine, systematic review, meta-analysis

1 Introduction

Stroke is the third leading cause of death and disability globally, especially in low- and middle-income countries (GBD, 2019 Stroke Collaborators, 2021). From 1990 to 2019, the absolute number of global stroke events increased by 70.0%, and stroke mortality increased by 43.0% worldwide (GBD, 2019 Stroke Collaborators, 2021). Stroke patients often have motor dysfunction, loss of activities of daily living (ADL) (Jørgensen et al., 1999), and a significant decline in quality of life, which prevents them from returning to work, thereby resulting in economic losses for the country's productivity (Rochmah et al., 2021). According to the American Heart Association, the total cost of stroke, including direct and indirect expenditures, is projected to increase from \$105.2 billion in \$2012 to \$240.7 billion in 2030 (Ovbiagele et al., 2013).

Acute ischemic stroke (AIS) accounts for most of all strokes. The appropriate treatment for AIS is significantly associated with prognosis (Hasan et al., 2021; Rosa et al., 2022). The primary therapeutic goal of AIS is to restore perfusion of ischemic brain tissue, and the main treatments include intravenous thrombolysis (IVT) and/or endovascular thrombectomy (EVT) (Hasan et al., 2021). However, 3%-8% of patients receiving IVT experience symptomatic cerebral hemorrhage (Gumbinger et al., 2012). Due to the narrow time window, contraindications, and the relatively low recanalization rate of large artery occlusions, the number of AIS patients who benefit from IVT is not as large as expected (Bhatia et al., 2010). EVT can significantly improve the prognosis of stroke; however, most interventional neuroradiologists work in urban areas, while half of the world's population lives in rural areas, resulting in limited access to EVT (Wassélius et al., 2022). Therefore, it is necessary to find an effective and safe therapy with a longer time window to improve the prognosis of stroke and address its burden.

Shuxuening injection (SXNI) extracted from *Ginkgo biloba* is a commercial Chinese polyherbal preparation that is widely used for stroke in China (Cui et al., 2020; Li et al., 2023). SXNI can dilate blood vessels and improve blood circulation, and it is mainly used for ischemia cardio-cerebrovascular diseases, such as cerebral infarction, vasospasm and coronary heart disease. The

pharmacologically active metabolites of SXNI are flavonol glycosides and ginkgolide (Smith et al., 1996; Shi et al., 2009). Numerous in vitro and in vivo studies have confirmed the neuroprotective effect of G. biloba extract (GBE) (Oyama et al., 1996; Guidetti et al., 2001; Ahlemeyer and Krieglstein, 2003). GBE can improve blood circulation, strengthen capillary walls, prevent thrombosis, and protect nerve cells from damage during hypoxia (Singh et al., 2019). Two studies (Oskouei et al., 2013; Li et al., 2017) showed that GBE was better than placebo or aspirin in improving stroke patients' neurological function, as assessed by the National Institutes of Health Stroke Scale (NIHSS). More interestingly, GBE can work within 1-3 h (Diamond et al., 2000). Compared with IVT or EVT, SXNI not only has a longer treatment time window and cheaper costs with fewer side effects (Li et al., 2023) but can also be implemented in urban and rural medical places without specially higher professional requirements for doctors. However, due to the complexity of the metabolites of SXNI, it requires more careful monitoring for patients to prevent adverse events (AEs) while administering the drug.

Previous systematic reviews published in 2011, 2012, and 2016 confirmed the efficacy of SXNI for treating AIS in terms of the clinical efficacy assessed by the clinical effective rate (CER), with a very low level of evidence. However, some outcomes that are conducive to assessing the overall status of stroke patients, such as neurological function assessed by internationally recognized tools (e.g., the NIHSS), activities of daily living (ADL), and AEs, were not reported in these reviews. In addition, numerous RCTs on SXNI for AIS have been published since 2016, and it is necessary to update the evidence. We aimed to comprehensively assess the efficacy and safety of SXNI as an add-on therapy for AIS in terms of clinical efficacy, neurological function, ADL, and AEs.

2 Methods

This study was conducted strictly following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Page et al., 2021). The protocol was registered at PROSPERO (www. crd.york.ac.uk), and the registration number was CRD42023418565.

2.1 Types of studies

All RCTs about SXNI for AIS were eligible for inclusion. The language of publication was not limited. We excluded case-control studies, retrospective studies, case reports, animal experiments, cell experiments, reviews, meta-analyses, clinical experiences, commentaries, and conference abstracts.

2.2 Participants

Patients who were older than 18 years and diagnosed with AIS according to the recognized guidelines or criteria and confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) were included without limitations on sex, culture, nationality, or race. The duration of the stroke should have been less than 14 days. We excluded patients with hypoxic-ischemic encephalopathy and *postpartum* apoplexy.

2.3 Types of interventions

The SXNI group received SXNI combined with conventional treatments (CTs), and the non-SXNI group received CTs alone or CTs combined with other injections. According to the Chinese guidelines for the diagnosis and treatment of AIS 2018; Chinese Society of Neurology Chinese Stroke Society, 2018), CTs include IVT, EVT, antiplatelet drugs, neuroprotective agents, and symptomatic supportive treatment, such as the management of blood pressure and blood lipid and sugar levels. Other injections were defined as any monodrug of non-Ginkgo biloba extract, such as compound Danshen injection, Shuxuetong injection, and so on. The duration of treatment had to be between 14 and 30 days. There were no restrictions on daily dose or frequency.

2.4 Outcome measures

The primary outcome was clinical efficacy assessed by the CER. According to the scoring criteria for clinical neurological deficit (CND) in stroke patients (Fourth Session of Chinese National Cerebrovascular Conference, 1996), improvements in CND were classified into five categories: a) recovery: 90%–100% reduction in CND with a disability level of 0; b) significant improvement: 46%–89% reduction in CND with a disability level of 1–3; c) progress: 18%–45% reduction in CND; d) inefficacy: less than 17% reduction in CND; e) deterioration: greater increase in CND. CER = (a + b + c) cases/total cases × 100% (National Administration of Traditional Chinese Medicine, 1994; Zheng, 2002).

The secondary outcomes included a) neurological function assessed by the Chinese Stroke Scale (CSS) and the NIHSS; b) ADL assessed by the Barthel Index (BI); c) AEs. The CSS consists of eight dimensions with a total score of 45. A higher CSS score indicates that a patient's stroke is more severe (Fourth Session of Chinese National Cerebrovascular Conference, 1996). The NHISS consists of 15 items with a total score of 42 and is a validated tool for assessing the severity of acute stroke. The greater the NIHSS score is, the more severe the neurological deficit (Brott et al., 1989; Kwah and Diong, 2014). The highest BI score is 100, and the higher the BI score is, the better the individual's ability to perform ADLs (Mahoney and Barthel, 1965). The common AEs related to SXNI are headache, flushing, and so on.

2.5 Data sources and searches

Seven databases were searched from their inception to January 2023, including PubMed, the Cochrane Library, Embase, the China National Knowledge Infrastructure (CNKI), the WanFang Database, the Chinese Scientific Journal Database (VIP), and the Chinese Biological Medicine Database (CBM). We also searched the Chinese Clinical Trial Registry (http://www.chictr.org.cn/) and the U.S. Clinical Trial Registry (https://clinicaltrials.gov/). We screened the reference lists of all included studies to identify more eligible studies. The search terms included ("stroke" OR "palsy" OR "apoplexy" OR "apoplexia" OR "cerebrovascular disorders" OR "cerebral infarction" OR "infarct of brain" OR "cerebral hemorrhage" OR "intracerebral hemorrhage" OR "brain hemorrhage") AND ("shuxuening" OR "shuxuening injection" OR "Ginkgo Leaf" OR "Folium Ginkgo" OR "Chinese patent medicine"). The detailed search strategy is described in Supplementary Appendix 1.

2.6 Selection of studies

We not only removed reduplicated articles using NoteExpress 3.6 but also performed manual de-duplication. Then, two reviewers independently screened the literature based on predefined eligibility criteria. We first excluded irrelevant literature by reading the titles and abstracts and then reading the full texts to select eligible studies. When two or more studies reported the same RCT, we selected the study with the largest sample size, appropriate outcomes, and the earliest publication. We consulted a third reviewer to resolve any disagreements.

2.7 Data extraction and management

We developed standardized data extraction forms that included study information (e.g., author, publication year, city, and country), characteristics of participants (e.g., age, sex, and course of stroke), study design (e.g., sample size, interventions, administration methods, duration of intervention, and SXNI manufacturing company), and outcomes (e.g., CER, NIHSS, CSS, BI, and AEs). Two reviewers extracted the data independently and cross-checked the extracted data. We contacted the authors via email when the information in the article was unclear or insufficient. If there were disagreements on data extraction, a third reviewer was consulted.

2.8 Quality assessment

The quality of the included studies was evaluated by two reviewers using the Cochrane risk of bias (ROB) assessment tool (Higgins and Green, 2011). The ROB tool includes seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Each item can be judged as "low risk", "high risk" or "unclear risk". If a study had a "low risk" of more than four domains, its overall quality was judged as high. Any disagreements between the two reviewers were resolved by a third reviewer.

2.9 Data synthesis

We used R software (version 4.1.2, https://cran.r-project.org/) and Review Manager software (version 5.4, Cochrane Collaboration, Copenhagen, Denmark) to analyze the data. Dichotomous data are expressed as risk ratios (RRs) and 95% confidence intervals (CIs). Continuous data assessed using the same scale are expressed as weighted mean differences (WMDs) and 95% CIs, whereas standardized mean differences (SMDs) and 95% CIs were used for the different scales. Statistical heterogeneity was assessed by I^2 and p values from the Cochrane Q test. $I^2 < 50\%$ and $p \ge 0$. 05 indicated no heterogeneity existed; otherwise, the fixed effects model was used if heterogeneity existed; otherwise, the fixed effects model was used. p < 0.05 was considered to indicate a statistically significant difference.

2.10 Sensitivity analysis

We tested the stability of the meta-analysis results by alternating the random and fixed effects models. Moreover, we excluded each study in turn to test the robustness of the results.

2.11 Subgroup analysis

We performed a subgroup analysis based on the duration of intervention, daily dose, and different injections used in the control group. We also conducted mixed-effects meta-regression analysis using sample size (n \leq 107 vs. n > 107), quality of studies (high vs. low), publication year, mean age (\leq 60 years old vs. > 60 years old vs. mixed), and total dose of SXNI (\leq 280 mL vs. > 280 mL) as covariates to search for sources of heterogeneity.

2.12 Publication bias

Publication bias was assessed with "funnel" and Egger's tests when the number of included studies was more than 10.

2.13 Quality of evidence

We evaluated the quality of evidence for each outcome using the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) tool (https://www.gradepro.org/). The GRADE included five domains: a) risk of bias, b) inconsistency, c) indirectness, d) imprecision, and e) other considerations, such as publication bias and number of included studies. The overall level of

evidence for every outcome was judged as high, moderate, low, or very low. Any disagreement regarding the level of evidence was resolved through discussion and consultation.

3 Results

3.1 Study selection

A total of 4,061 records were retrieved, 2075 of which were duplicate publications. After removing 1,775 records that did not meet the criteria by screening the titles and abstracts, we read the full texts of 211 articles. Finally, 116 eligible studies were included in the meta-analysis. The details of the study selection process are displayed in Figure 1. The full citation details of the included and excluded studies are described in Supplementary Appendix 2.

3.2 Characteristics of the included studies

All included studies were conducted in China and published in Chinese, with publication years distributed between 2002 and 2023. The most frequent provinces of author affiliation were Henan, Shandong, Guangdong, and Hebei. The sample sizes were between 40 and 438, and the duration of AIS ranged from less than 12 h to 14 days. The intervention duration ranged from 14 to 30 days. The daily dose of SXNI varied from 2 to 30 mL. The total dose of SXNI was between 28 and 900 mL. Thirty-six studies with 3,568 participants compared the efficacy of SXNI plus CTs vs. CTs alone, and eight studies with 8,833 participants compared the efficacy of SXNI plus CTs vs. CTs plus other injections. Of the 116 studies, 102 reported the CER, 14 reported the BI, 44 reported the CSS, and 16 reported the NIHSS. The characteristics of the included studies are described in Table 1.

3.3 The quality of the included studies

Fifteen (12.9%) studies were judged to be of moderate to high quality (Table 2; Figure 2). Of 116 studies, 110 (94.8%) mentioned the word "randomization", 15 (12.9%) used random number table methods, and the remaining studies used incorrect or undetailed randomization methods. Five (4.3%) studies mentioned the word "blinding" without a detailed description of the specific methods. None of the studies reported allocation concealment. Three (2.6%) studies were judged as high risk because they did not conduct intention-to-treat analysis and did not specify the reason for case dropout. Nine (7.8%) studies were assessed as high risk for selective reporting based on the description of the methods in the article. All included studies were free of other sources of ROB.

3.4 Primary outcome

3.4.1 Clinical efficacy

3.4.1.1 SXNI plus CTs vs. CTs alone

Thirty-two studies with 3,056 participants reported the CER. We used a fixed effects model due to the low heterogeneity ($I^2 = 0\%$, p =

Study	Study sites	Sample size	Time sind	ce stroke	Ag		Se (M	ex /F)	In	terventions	Daily dose of	Intervention duration	SXNI manufacturing	Outcomes
		T/C	т	С	Т	С	т	С	т	С	SXNI		company	
Cao M 2004	Hebei, China	35/40	11h-6d	12h-7d	41-78	43-76	22/ 13	26/ 14	SXNI + CTs	CTs + Compound Danshen injection	15 ml, qd, ivgtt	14 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER, AEs
Cao XM 2015	Hebei, China	56/56	10-28h	10-28h	60 ± 1.2	60 ± 1.2	NR	NR	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS
Chang CF 2015	Henan, China	150/128	6-72h	6-72h	64.9	63.7	98/ 52	84/ 44	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, BI, AEs
Che YQ 2005	Liaoning, China	46/44	6-72h	6-72h	50-76	48-78	29/ 17	34/ 10	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	Xiamen Pengdao Pharmaceutical Co., Ltd	CER, CSS, AE
Chen JJ 2014	Jiangsu, China	30/30	48h-1w	48h-1w	61 ± 5.26	62 ± 5.77	20/ 10	18/ 12	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Chen LY 2021	Hunan, China	35/35	<3d	<3d	57.84 ± 1.55	56.68 ± 1.39	20/ 15	18/ 17	SXNI + CTs	CTs + Edaravone injection	2 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	NIHSS, BI
Chen R 2015	Jiangsu, China	39/39	32.47 ± 6.52h	32.47 ± 6.52h	65.38 ± 7.49	65.38 ± 7.49	NR	NR	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	28 d	NR	CSS
Chen YF 2009	Shanghai, China	40/40	1-5d	1-5d	74.60 ± 7.53	72.95 ± 7.37	16/ 24	13/ 27	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER
Chen ZC 2014	Guangdong, China	34/34	12-72 h	12-72 h	61.6 ± 4.3	58.6±5.3	22/ 12	18/ 16	SXNI + CTs	CTs + Chuanxiongqin injection	20 ml, qd, ivgtt	14 d	SHIYAO YINHU PHARMACENRTICAL CO., LTD	CER, AEs
Cheng ZL 2016	Hebei, China	40/40	15.4 ± 4.8h	16.1 ± 5.2h	58.7 ± 7.2	60.1 ± 6.8	25/ 15	23/ 17	SXNI + CTs	CTs	10 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER
Cui YM 2014	Henan, China	62/62	≤48 h	≤48 h	62.8 ± 12.6	62.8 ± 12.6	NR	NR	SXNI + CTs	CTs + Venoruton injection	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER
Dai YP 2008	Henan, China	80/80	l-7d	l-7d	38-82	40-81	44/ 36	47/ 33	SXNI + CTs	CTs + Venoruton injection	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER, AEs
Du PK 2016	Henan, China	49/49	6.1 ± 1.9d	6.5 ± 1.4d	61.2 ± 3.7	63.1 ± 4.0	31/ 18	29/ 20	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	Heilongjiang Zbd Pharmaceutical Co., Ltd	CER, CSS

10.3389/fphar.2024.1407669

Study	Study sites	Sample size	Time sind	ce stroke	Ag		Se (M	ex ∕F)	Int	terventions	Daily dose	Intervention duration	SXNI manufacturing	Outcomes
		T/C	т	С	т	С	т	С	т	С	of SXNI		company	
Du XL 2010	Beijing, China	99/99	1.7 ± 0.5d	1.9 ± 0.3d	69.1 ± 4.4	67.3 ± 3.7	54/ 50	51/ 51	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	NIHSS, AEs
Feng JW 2017	Shandong, China	47/47	6.15 ± 1.29h	6.02 ± 1.26h	56.89 ± 12.67	58.05 ± 10.38	26/ 21	27/ 20	SXNI + CTs	CTs + Danshen injection	30 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER
Gao YD 2011	Zhejiang, China	60/60	<72h	<72h	45-85	46-87	39/ 21	40/ 20	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AEs
Ge J 2013	Henan, China	70/67	6-24h	6-24h	61.23 ± 12.98	60.88 ± 11.75	39/ 31	38/ 29	SXNI + CTs	CTs + Compound Danshen injection	10 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd.	CER, AEs
Guo WJ 2013	Hebei, China	35/35	l-3d	l-3d	58.38 ± 4.27	61.32 ± 5.88	20/ 15	19/ 16	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER, AEs
He J 2010	Anhui, China	40/40	1-3d	1-3d	58-72	59-74	32/8	28/ 12	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	30 d	NR	CER, AEs
He JQ 2013	Guangdong, China	39/39	<12h	<12h	71.2 ± 2.3	72.1±2.1	30/9	31/8	SXNI + CTs	CTs	10 ml, qd, ivgtt	20 d	NR	CER
He XY 2006	Sichuan, China	30/30	<12h	<12h	78.69 ± 6.21	78.69 ± 6.21	NR	NR	SXNI + CTs	CTs	25 ml, qd, ivgtt	15 d	NR	CER, AEs
Hua GC 2002	Shanghai, China	60/32	36 ± 0.4h	35 ± 0.6h	69 ± 3.2	68 ± 4.1	36/ 24	17/ 15	SXNI + CTs	CTs + Ginaton injection	25 ml, qd, ivgtt	15 d	Beijing Wanhui Pharmaceutical Group	AEs
Huang DL 2009	Guangdong, China	40/40	12-96h	12-96h	38-72	39-71	27/ 13	28/ 12	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Huang JL 2010	Shaanxi, China	60/60	30 min-42 h	1-39 h	55.2 ± 8.5	56.6 ± 7.9	35/ 25	37/ 23	SXNI + CTs	CTs	20 ml, qd, ivgtt	28 d	Boan Brothers Pharmaceutical Co., Ltd	ESS, CER, BI
Huang M 2004	Guangdong, China	30/30	6 h-3 d	6 h-3 d	65.3 ± 7.5	64.2 ± 8.1	18/ 12	20/ 10	SXNI + CTs	CTs + Compound Danshen injection	10 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CSS
Huang XZ 2014	Fujian, China	64/60	<14d	<14d	86.7 ± 3.6	87.7 ± 2.8	44/ 20	38/ 22	SXNI + CTs	CTs + Rhadiola extract injection	20 ml, qd, ivgtt	14 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd	CER, AEs
Jia HB 2008	Liaoning, China	62/61	12-72h	12-72h	43-85	42-86	39/ 23	37/ 24	SXNI + CTs	CTs + Chuanxiongqin injection	20 ml, qd, ivgtt	14 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd	CER, CSS, AEs

Study	Study sites	Sample size	Time sine	ce stroke	Ag	e	Se (M	ex /F)	Int	erventions	Daily dose of	Intervention duration	SXNI manufacturing	Outcomes
		T/C	т	С	т	С	т	С	т	С	SXNI		company	
Jia HY 2021	Henan, China	41/41	11.52 ± 1.47h	11.74 ± 1.51h	57.38 ± 4.67	57.95 ± 4.16	22/ 19	23/ 18	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	NR	NIHSS, CER
Jiang BN 2009	Shandong, China	55/55	<72h	<72h	67 ± 8.31	70 ± 9.14	35/ 20	33/ 22	SXNI + CTs	CTs + Xuesaitong injection	10 ml, qd, ivgtt	21 d	Tonghua Guhong Pharmaceutical Co., Ltd	CER, CSS
Jiao XL 2008	Zhejiang, China	30/22	3h-7d	3h-7d	46-89	46-89	NR	NR	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	28 d	NR	CER
Ji DY 2014	Shaanxi, China	62/60	8-28h	7-29h	41-77	40-78	38/ 24	36/ 24	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Kou XF 2012	Henan, China	50/50	<72h	<72h	66.7 ± 9.3	66.7±9.3	NR	NR	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	NIHSS, CER, AEs
Lei GR 2014	Jiangxi, China	45/45	18.3 ± 5.1h	18.3 ± 5.1h	59.21 ± 7.4	59.21 ± 7.4	NR	NR	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER
Li JH 2008	Beijing, China	44/44	<48h	<48h	61-82	61-80	32/ 12	34/ 10	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AEs
Li SJ 2014	Shaanxi, China	60/60	≤72h	≤72h	63.8 ± 1.5	63.8 ± 1.5	NR	NR	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, BI, AEs
Li XF 2014	Shandong, China	48/42	2.1 ± 1.0h	2.2 ± 1.2h	63.7 ± 5.9	64.1 ± 6.3	26/ 22	22/ 20	SXNI + CTs	CTs	20 ml, qd, ivgtt	28 d	NR	CSS
Li XH 2011	Jilin, China	120/120	≤7d	≤7d	42-78	40-77	NR	NR	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	SHIYAO YINHU PHARMACENRTICAL CO., LTD	CER, CSS
Li XJ 2010	Sichuan, China	28/30	3.78 ± 1.96d	4.08 ± 2.11d	63.5 ± 4.3	62.8 ± 4.6	18/ 10	19/ 11	SXNI + CTs	CTs + Xuesaitong injection	20 ml, qd, ivgtt	14 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER, CSS
Li XL 2023	Jiangsu, China	35/35	<14d	<14d	63.79 ± 4.83	63.02 ± 4.57	23/ 12	25/ 10	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	NIHSS, CER, B
Li XR 2011	Guizhou, China	90/60	<72h	<72h	50.8 ± 8.7	60.7 ± 9.5	39/ 51	26/ 34	SXNI + CTs	CTs	10 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CSS
Li YJ 2018	Hebei, China	62/62	6-72h	6-72h	58.6 ± 3.4	59.2 ± 3.5	32/ 30	34/ 28	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd	NIHSS, CER, B

Study	Study sites	Sample size	Time sine	ce stroke	Ag	e	Se (M	ex /F)	In	terventions	Daily dose	Intervention duration	SXNI manufacturing	Outcomes
		T/C	т	С	т	С	т	С	т	С	of SXNI		company	
Li ZY 2013	Neimenggu, China	80/80	9-72h	9-72h	41-76	41-76	NR	NR	SXNI + CTs	CTs + Troxerutin injection	20 ml, qd, ivgtt	15 d	NR	NIHSS, CER, AEs
Lin YQ 2006	Guangdong, China	50/50	48h-1w	48h-1w	35-79	40-82	27/ 23	30/ 20	SXNI + CTs	CTs + Venoruton injection	6 ml, qd, ivgtt	15 d	NR	CER, AEs
Ling YX 2006	Guangdong, China	220/218	8.2 ± 4.5h	8.3 ± 4.8h	56.5 ± 21.5	57.2 ± 22.4	124/ 96	120/ 98	SXNI + CTs	CTs + Compound Danshen injection	12 ml, qd, ivgtt	15 d	NR	CER, AEs
Liu JX 2004	Shaanxi, China	60/46	1-5d	1-6d	41-83	42-84	32/ 28	24/ 22	SXNI + CTs	CTs	30 ml, qd, ivgtt	30 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd.	CER
Liu JX 2010	Tianjin, China	50/50	<72h	<72h	45-75	45-75	NR	NR	SXNI + CTs	CTs + Xuesaitong injection	20 ml, qd, ivgtt	14 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd	CER, AEs
Liu MF 2009	Henan, China	60/60	≤3d	≤3d	63.9 ± 8.7	63.9 ± 8.7	NR	NR	SXNI + CTs	CTs + Compound Danshen injection	16 ml, qd, ivgtt	14 d	NR	CER, AEs
Liu S 2004	Shandong,China	60/60	1-3d	1-3d	45-78	45-78	34/ 26	38/ 22	SXNI + CTs	CTs + Venoruton injection	12 ml, qd, ivgtt	14 d	Sanjiu Enterprise Group(Shenzhen Nanfang Pharmaceutical Plant)	AEs
Liu XH 2013	Hunan, China	82/82	≤12h	≤12h	77.8±9.2	76.5±8.7	75/7	76/6	SXNI + CTs	CTs + Compound Danshen injection	25 ml, qd, ivgtt	30 d	NR	CER
Liu XJ 2008	Liaoning, China	68/30	≤7d	≤7d	36-80	36-80	41/ 27	17/ 13	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Liu XY 2016	Neimenggu, China	47/47	4.92 ± 1.21h	4.86 ± 1.12h	64.39 ± 9.26	64.28 ± 9.17	27/ 20	25/ 22	SXNI + CTs	CTs + Shuxuetong injection	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER, CSS
Liu Y 2003	Jiangsu, China	56/48	≤48h	≤48h	<75	<75	NR	NR	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER
Ma YX 2016	Jilin, China	43/43	2.18 ± 0.41d	2.34 ± 0.42d	60.34 ± 5.28	60.23 ± 5.32	24/ 19	23/ 20	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, BI
Mai Y 2005	Yunnan, China	34/30	1-5d	1-5d	61-84	63-86	28/6	25/5	SXNI + CTs	CTs	20 ml, qd, ivgtt	30 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, CSS, AE
Nie XP 2020	Jiangxi, China	44/44	4.62 ± 1.79h	4.57 ± 1.62h	66.8 ± 2.5	66.4 ± 2.6	22/ 22	20/ 24	SXNI + CTs	CTs	20 ml, qd, ivgtt	20 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd	CER, AEs

Study	Study sites	Sample size	Time sine	ce stroke	Ag	e	Se (M	ex /F)	In	terventions	Daily dose	Intervention duration	SXNI manufacturing	Outcomes
		T/C	Т	С	т	С	т	С	т	С	of SXNI		company	
Peng J 2021	Hunan, China	37/37	4.21 ± 0.57h	4.39 ± 0.66h	64.25 ± 0.37	64.53 ± 0.84	20/ 17	21/ 16	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	Shanxi Taiyuan Pharmaceutical Co., Ltd	NIHSS, BI
Qin DY 2014	Guangxi, China	30/30	6-24h	6-24h	42-78	45-76	20/ 10	18/ 12	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER, CSS
Qin QA 2013	Henan, China	120/116	9-28h	10-29h	41-75	40-76	76/ 44	70/ 46	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AE
Ren JM 2006	Jiangsu, China	38/34	≤48h	≤48h	64±8	62±7	20/ 18	18/ 16	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Shang S 2014	Henan, China	44/44	<72h	<72h	37-81	36-79	27/ 17	26/ 18	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	15 d	NR	CER, AEs
Shen DD 2017	Zhejiang, China	57/57	16.1 ± 4.12h	15.67 ± 3.78h	62.34 ± 4.01	61.46 ± 3.69	33/ 24	37/ 20	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	NR	NIHSS, CER, AEs
Shi JP 2008	Henan, China	41/41	48-72h	48-72h	40-79	37-78	26/ 15	24/ 17	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	15 d	Guizhou Yibai Pharmaceutical Co., Ltd	CER, CSS, AE
Su HM 2007	Shanghai, China	36/32	8h-6d	9h-5d	53.5	55	22/ 14	21/ 11	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	15 d	NR	CER
Sun BJ 2014	Hebei, China	100/100	36.5 ± 13.5h	39.5 ± 16.3h	60.5 ± 14.6	63.5 ± 14.6	55/ 45	54/ 46	SXNI + CTs	CTs + Shuxuetong injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS
Sun HY 2005	Zhejiang, China	52/51	9h-3d	9h-3d	39-78	41-77	34/ 18	32/ 19	SXNI + CTs	CTs + Danshen injection	12 ml, qd, ivgtt	15 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd.	CER, CSS, AE
Sun T 2019	XinJiang, China	20/20	≤24h	≤24h	59.4 ± 6.7	59.4 ± 6.7	NR	NR	SXNI + CTs	CTs + Compound Xueshuantong injection	20 ml, qd, ivgtt	14 d	Heilongjiang Zbd Pharmaceutical Co., Ltd	NIHSS, CER, AEs
Tai SEGL 2011	Xinjiang, China	60/60	≤3d	≤3d	58-86	56-86	48/ 12	47/ 13	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	30 d	NR	CER, CSS
Tian ZC 2008	Shandong, China	56/24	1-10d	1-10d	62 ± 3.72	64.1 ± 3.86	NR	NR	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	21 d	NR	CSS, AEs
Wang DH 2023	Beijing, China	60/60	26.14 ± 5.32h	25.32 ± 4.94h	57.32 ± 8.56	58.59 ± 7.88	35/ 25	33/ 27	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	SHIYAO YINHU PHARMACENRTICAL CO., LTD	NIHSS, CER, BI, AEs

Study	Study sites	Sample size	Time sine	ce stroke	Ag	e		ex /F)	In [:]	terventions	Daily dose	Intervention duration	SXNI manufacturing	Outcome
		T/C	т	С	т	С	т	С	т	С	of SXNI		company	
Wang HL 2013	Beijing, China	40/40	19.1 ± 10.6h	18.6 ± 9.9h	66.7 ± 8.5	67.4 ± 9.1	22/ 18	23/ 17	SXNI + CTs	CTs + Edaravone injection	20 ml, qd, ivgtt	14 d	Heilongjiang Zbd Pharmaceutical Co., Ltd.	NIHSS, CER
Wang HR 2010	Chongqing, China	53/53	1-65h	0.5-61h	43-77	41-78	24/ 29	21/ 32	SXNI + CTs	CTs	20 ml, qd, ivgtt	28 d	Boan Brothers Pharmaceutical Co., Ltd	CER, CSS
Wang JF 2018	Shandong, China	32/32	15.27±4.24h	15.34±4.11h	70.41±1.33	70.34 ± 1.41	21/ 11	20/ 12	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	SHIYAO YINHU PHARMACENRTICAL CO., LTD	CER
Wang MS 2012	Henan, China	106/106	<48h	<48h	67.4 ± 8.7	69.0 ± 9.8	70/ 36	68/ 38	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Wang QY 2012	Shanxi, China	40/40	<72h	<72h	48-67	44-70	27/ 13	25/ 15	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AB
Wang SW 2014	Guangxi, China	31/30	0.5-7d	1-7d	49-78	50-77	20/ 11	21/9	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	15 d	NR	CER, CSS, AF
Wang WH 2006	Sichuan, China	30/30	<12h	<12h	78.69 ± 6.21	78.69 ± 6.21	NR	NR	SXNI + CTs	CTs	25 ml, qd, ivgtt	15 d	NR	CER, AEs
Wang XH 2015	Henan, China	51/51	4.01 ± 0.22d	4.01 ± 0.22d	62.1 ± 2.3	62.1 ± 2.3	NR	NR	SXNI + CTs	CTs + Xuesaitong injection	20 ml, qd, ivgtt	14 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER, CSS
Wu J 2011	Henan, China	33/31	6h-3d	6h-3d	55.42 ± 11.72	56.03 ± 12.49	17/ 16	15/ 16	SXNI + CTs	CTs + Edaravone injection	16 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, CSS
Wu XJ 2006	Hunan, China	30/30	1-3d	1-3d	65.80 ± 8.62	65.40 ± 8.40	16/ 14	17/ 13	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	Shanxi Zhendong Taisheng Pharmaceutical Co., Ltd	CER, AEs
Wu Y 2011	Guangdong, China	30/30	6-72h	6-72h	60.21 ± 8.72	60.21 ± 8.72	NR	NR	SXNI + CTs	CTs	10 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, AEs
Wu ZX 2004	Zhejiang, China	50/34	1-2d	1-2d	36-70	40-72	27/ 23	15/ 19	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, AEs
Xiao DF 2022	Liaoning, China	40/40	18.02 ± 2.57h	17.96 ± 2.64h	66.84 ± 4.93	67.03 ± 5.22	21/ 19	22/ 18	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	Heilongjiang Zbd Pharmaceutical Co., Ltd	NIHSS, CER, BI, AEs
Xie RP 2010	Shanxi, China	40/40	12-72h	12-72h	42-80	42-80	NR	NR	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	15 d	China Shineway Pharmaceutical Group Limited	CER, AEs

Zhan et al.

Study	Study sites	Sample size	Time sind	ce stroke	Ag	e	Se (M	ex /F)	Int	terventions	Daily dose	Intervention duration	SXNI manufacturing	Outcomes
		T/C	т	С	т	С	т	С	т	С	of SXNI		company	
Xie YQ 2004	Hunan, China	30/30	<7d	<7d	59.4	57.7	17/ 13	18/ 12	SXNI + CTs	CTs	25 ml, qd, ivgtt	15 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER, CSS, BI, AEs
Xin FB 2005	Hubei, China	121/121	<24h	<24h	58 ± 8	60 ± 7	76/ 45	71/ 50	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, CSS, AEs
Xiong SC 2011	Sichuan, China	40/40	5-22h	4-24h	51-75	50-72	22/ 28	23/ 17	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	20 d	NR	CER, CSS
Xu CY 2012	Shandong, China	60/60	<7d	<7d	41-82	40-81	32/ 28	38/ 22	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	SHANGHAI ASIA PIONEER PHARMACENRTICAL CO., LTD	AEs
Xu L 2008	Henan, China	30/30	8h-1w	8h-1w	55.42 ± 11.72	56.03 ± 12.49	18/ 12	19/ 11	SXNI + CTs	CTs + Sodium Ozagrel injection	16 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, CSS, AEs
Xu PF 2011	Guangdong, China	35/35	1-5d	1.05-5d	65 ± 9.2	66.8 ± 10.3	19/ 16	20/ 15	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	Heilongjiang Zbd Pharmaceutical Co., Ltd	CER, AEs
Xue JY 2013	Henan, China	24/24	4.5 ± 1.8h	4.5 ± 1.8h	65.8 ± 5.2	65.8 ± 5.2	NR	NR	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER
Yan TQ 2016	Shandong, China	45/45	12.4 ± 1.6h	14.1 ± 1.8h	54.2 ± 2.4	53.5 ± 2.5	25/ 20	23/ 22	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	NR	CER
Yan XY 2010	Anhui, China	30/30	6-72h	6-72h	52.13 ± 9.71	58.32 ± 8.79	18/ 12	16/ 14	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER, AEs
Yang JH 2010	Hunan, China	48/48	<7d	<7d	46-75	47-75	26/ 22	25/ 23	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Yang M 2009	Anhui,China	30/30	<7d	<7d	66.3 ± 9.3	67.4 ± 8.6	NR	NR	SXNI + CTs	CTs + Sodium Ozagrel injection	20 ml, qd, ivgtt	14 d	NR	CER, AEs
Yang XW 2006	Guangdong, China	46/35	<48h	<48h	46-74	45-75	28/ 18	21/ 14	SXNI + CTs	CTs + Compound Xueshuantong injection	10 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, AEs
Yin HX 2004	Guangdong, China	95/90	<48h	<48h	35-78	38-76	68/ 27	65/ 25	SXNI + CTs	CTs + Compound Danshen injection	10 ml, qd, ivgtt	14 d	Langzhi Group Wanrong Pharmaceutical Co., Ltd	CER, CSS, AEs
Yin ZL 2020	Jilin, China	34/34	12.46 ± 1.61h	12.48 ± 1.62h	56.17 ± 3.24	56.14 ± 3.26	20/ 14	19/ 15	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	Tonghua Guhong Pharmaceutical Co., Ltd	NIHSS, CER

Zhan et al.

10.3389/fphar.2024.1407669

Study	Study sites	Sample size	Time sine	ce stroke	Ag		Se (M	ex /F)	Int	terventions	Daily dose	Intervention duration	SXNI manufacturing	Outcomes
		T/C	Т	С	т	С	т	С	т	С	of SXNI		company	
Yu BQ 2003	Jiangsu, China	66/75	11h-6d	11h-7d	67 ± 11.5	64 ± 12.4	42/ 36	49/ 41	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, BI, AEs
Zang ZX 2010	Heilongjiang, China	65/62	9-72h	8-72h	62.5 ± 10.3	63.4 ± 9.89	41/ 24	38/ 24	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	CER, CSS
Zhang GJ 2010	Heilongjiang, China	124/122	12-72h	12-72h	41-83	41-83	78/ 46	74/ 48	SXNI + CTs	CTs + Chuanxiongqin injection	20 ml, qd, ivgtt	14 d	NR	AEs
Zhang H 2009	Hubei, China	60/58	9-28h	10-29h	42-76	41-77	38/ 22	35/ 23	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	Beijing China Rescources High-Tech Natural Pharmaceutical Co., Ltd	CER, CSS, BI, AEs
Zhang HM 2004	Shandong, China	74/70	<7d	<7d	54-80	56-79	NR	NR	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AEs
Zhang HX 2006	Hebei, China	110/100	16.1 ± 8.4h	16 ± 8.5h	62.56 ± 12.37	62.52 ± 12.4	56/ 54	51/ 49	SXNI + CTs	CTs + Venoruton injection	20 ml, qd, ivgtt	15 d	China Resources Double- crane Pharmaceutical Co., Ltd	ESS, AEs
Zhang L 2007	Jilin, China	40/40	<72h	<72h	44-78	44-78	NR	NR	SXNI + CTs	CTs + Xuesaitong injection	10 ml, qd, ivgtt	14 d	NR	CER, AEs
Zhang L 2010	Henan, China	40/40	48h-1w	48h-1w	35-74	42-78	23/ 17	24/ 16	SXNI + CTs	CTs + Venoruton injection	6 ml, qd, ivgtt	15 d	NR	CER, AEs
Zhang MX 2018	Shanghai, China	40/40	<48h	<48h	43-81	43-81	26/ 14	26/ 14	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS
Zhang RL 2008	Shaanxi, China	67/62	1-6d	NR	36-75	36-75	46/ 21	44/ 18	SXNI + CTs	CTs	20 ml, qd, ivgtt	30 d	NR	CER, CSS, AEs
Zhang XK 2017	Shandong, China	62/62	<3d	<3d	58.66 ± 7.25	57.59 ± 9.31	32/ 30	33/ 29	SXNI + CTs	CTs + Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AEs
Zhang XZ 2018	Henan, China	48/48	18.26 ± 2.32h	18.29 ± 2.30h	65.16 ± 4.62	65.19 ± 4.60	23/ 25	24/ 24	SXNI + CTs	CTs	20 ml, qd, ivgtt	14 d	China Shineway Pharmaceutical Group Limited	NIHSS, CER
Zhang YP 2004	Shanxi, China	66/58	6h-5d	6h-5d	45-78	42-80	38/ 28	35/ 23	SXNI + CTs	CTs + Compound Danshen injection	15 ml, qd, ivgtt	14 d	NR	CER, CSS
Zhao YX 2015	Henan, China	42/42	32.5 ± 9.4h	32.5 ± 9.4h	64.5 ± 8.1	64.5±8.1	NR	NR	SXNI + CTs	CTs + Edaravone injection	20 ml, qd, ivgtt	28 d	China Shineway Pharmaceutical Group Limited	NIHSS, BI, AE

Zhan et al

study	Study Study sites	Sample size	Time since stroke	ce stroke	Age	۵	Sex (M/F)	× Ĥ	Int	Interventions	Daily dose	Intervention duration	SXNI manufacturing	Outcomes
		T/C	F	U	F	U	F	υ	F	υ	ot SXNI		company	
Zheng YZ 2014	Henan, China	36/36	<72h	<72h	47-76	47-76	NR	NR	SXNI + CTs	CTs + Xueshuantong injection	10 ml, bid, ivgtt	21 d	Datong Huida Pharmaceutical Co., Ltd	CER, AEs
Zhu L 2014	Shaanxi, China	73/73	5-24h	6-24h	62.5 ± 13.1	61.8 ± 12.5	40/ 33	38/ 35	SXNI + CTs	CTs + Compound Danshen injection	20 ml, qd, ivgtt	14 d	NR	CER, CSS, AEs
Zhu XJ 2013	Liaoning, China	51/30	18.02 ± 4.28h	18.02 ± 4.28h	62.41 ± 4.24	60.38 ± 6.02	21/ 30	18/ 12	SXNI + CTs	CTs	25 ml, qd, ivgtt	14 d	China Resources Double- crane Pharmaceutical Co., Ltd	CER
Zhuang JS 2004	Hebei, China	77/71	15-72h	15-72h	64.2 ± 9.7	65.4 ± 8.1	NR	NR	SXNI + CTs	CTs + Venoruton injection	20 ml, qd, ivgtt	15 d	NR	CER, AEs
Zi XH 2004	Hunan, China	28/26	<7d	<7d	69.2 ± 5.3	70 ± 6.6	NR	NR	SXNI + CTs	CTs + Sodium Ozagrel injection	25 ml, qd, ivgtt	15 d	NR	CER, AEs

10.3389/fphar.2024.1407669

0.68). The meta-analysis results showed that SXNI plus CTs was superior to CTs alone in terms of the CER (RR: 1.21, 95% CI: 1.17-1.25, Z = 11.22, p < 0.05) (Figure 3A). Sensitivity analysis was conducted by adjusting the random and fixed effects models (Supplementary Table S1) or excluding each study in turn (Supplementary Figure S1), which demonstrated that the results were robust. Subgroup analysis revealed that the effects of different daily doses and different intervention durations of SXNI on CER were not significantly different between SXNI plus CTs and CTs alone (Supplementary Figures S2, S3). Mixed-effect meta-regression analysis further revealed that the sample size, mean age, total dose of SXNI, publication year, and quality of studies were not the main sources of heterogeneity (Supplementary Table S2). Egger's test (t =4.80, p < 0.05) and funnel plots revealed significant publication bias (Figure 4A).

3.4.1.2 SXNI plus CTs vs. CTs plus other injections

Seventy studies with 7,673 participants reported CER. A random effects model was used because of statistical heterogeneity ($I^2 = 25\%$, p < 0.05). The results of the meta-analysis showed that SXNI plus CTs was superior to CTs plus other injections in improving the CER (*RR*: 1.18, 95% *CI*: 1.15–1.21, Z = 13.26, p < 0.05) (Figure 3B). By adjusting the analysis models (Supplementary Table S1) or removing each study in turn (Supplementary Figure S4), sensitivity analysis indicated that the results were robust. Subgroup analysis revealed that the effects of different daily doses, different intervention durations, and different injections on CER were not significantly different between SXNI plus CTs and CTs plus other injections (Supplementary Figures S5-7). Mixedeffect meta-regression models did not reveal sample size, mean age, total dose of SXNI, publication year, or quality of studies as sources of heterogeneity (Supplementary Table S2). The results of Egger's test (t = 5.25, p < 0.05) and funnel plots showed publication bias (Figure 4B).

3.5 Secondary outcomes

3.5.1 Neurological function

3.5.1.1 SXNI plus CTs vs. CTs alone

Eleven studies, including 1,126 participants, assessed neurological function using the NIHSS. We used a random effects model due to the significant heterogeneity ($I^2 = 98\%$, p <0.05). SXNI plus CTs was superior for decreasing the NIHSS score compared with CTs alone (MD: -4.00, 95% CI: -5.22 to -2.78, Z = -6.42, p < 0.05) (Figure 5A). Sensitivity analysis was conducted by adjusting the random and fixed effects models (Supplementary Table S1) or deleting each study in turn (Supplementary Figure S8), which demonstrated that the meta-analysis results were robust. Mixed-effect meta-regression analysis revealed that the sample size, mean age, total dose of SXNI, publication year, and quality of studies did not contribute to the heterogeneity (Supplementary Table S2). Egger's test (t = -2.99, p < 0.05) and funnel plots revealed publication bias (Figure 4E).

Ten studies, including 1,117 participants, evaluated neurological function using CSS. Because of the significant heterogeneity (I^2 = 99%, p < 0.05), we used a random effects model to pool the data. SXNI plus CTs was superior to CTs alone for decreasing the CSS



(*MD*: -5.01, 95% *CI*: -7.38 to -2.65, Z = -4.15; p < 0.05) (Figure 5B). By adjusting the analysis models (Supplementary Table S1) or removing each study in turn (Supplementary Figure S9), sensitivity analysis indicated that the results were robust. Mixed-effect meta-regression analysis based on sample size, mean age, total dose of SXNI, publication year, and quality of studies did not reveal sources of heterogeneity (Supplementary Table S2). Egger's test (t = -0.36, p > 0.05) and funnel plots revealed no publication bias (Figure 4C).

3.5.1.2 SXNI plus CTs vs. CTs plus other injections

Five studies with 434 participants assessed neurological function via the NIHSS. Because of significant heterogeneity ($I^2 = 84\%$, p <0.05), we used a random effects model. The meta-analysis indicated that SXNI plus CTs improved the NIHSS score better than CTs plus other injections did (*MD*: -2.28, 95% *CI*: -3.41 to -1.16, Z = -3.97, p < 0.05) (Figure 5C). Sensitivity analysis was conducted by adjusting the random and fixed effects models (Supplementary Table S1) or deleting each study in turn (Supplementary Figure S10), which demonstrated that the meta-analysis results were robust. No source of heterogeneity was found in mixed-effect metaregression models based on sample size, mean age, total dose of SXNI, publication vear, or quality of studies (Supplementary Table S2).

Thirty-four studies involving 3,996 participants assessed neurological function using the CSS. A random effects model was used to pool the data due to the significant heterogeneity ($I^2 = 99\%$, p < 0.05). The results of the meta-analysis showed that SXNI plus CTs decreased the CSS score in AIS patients more than CTs plus

other injections did (*MD*: -4.31, 95% *CI*: -5.75 to -2.88, *Z* = -5.89, p < 0.05) (Figure 5D). By adjusting the analysis models (Supplementary Table S1) or removing each study in turn (Supplementary Figure S11), sensitivity analysis indicated that the results were robust. Subgroup analysis indicated that the effects of different daily doses, different intervention durations, and different injections on decreasing the CSS score were not significantly different between SXNI plus CTs and CTs plus other injections (Supplementary Figures S12–14). Mixed-effect meta-regression models revealed that sample size, mean age, total dose of SXNI, publication year, and quality of studies were not the main sources of heterogeneity (Supplementary Table S2). Egger's test (t = -1.20, p > 0.05) and funnel plots revealed no publication bias (Figure 4D).

3.5.2 Activities of daily living

3.5.2.1 SXNI plus CTs vs. CTs alone

Seven studies with 648 participants assessed ADLs using the BI. We used a random effects model to pool the data because of the substantial heterogeneity ($I^2 = 96\%$, p < 0.05). The meta-analysis showed that SXNI plus CTs was better at improving the BI score than CTs alone (*MD*: 11.58, 95% *CI*: 8.27–14.90, Z = 6.84, p < 0.05) (Figure 6A). By adjusting the analysis models (Supplementary Table S1) or removing each study in turn (Supplementary Figure S15), sensitivity analysis demonstrated the reliability of the results. Mixed-effect meta-regression analysis revealed that sample size, mean age, total dose of SXNI, publication year, and quality of studies were not the sources of heterogeneity (Supplementary Table S2).

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall quality
Cao M 2004	unclear	unclear	unclear	unclear	low	low	low	low
Cao XM 2015	unclear	unclear	unclear	unclear	low	low	low	low
Chang CF 2015	unclear	unclear	unclear	unclear	low	low	low	low
Che YQ 2005	unclear	unclear	unclear	unclear	low	low	low	low
Chen JJ 2014	unclear	unclear	unclear	unclear	low	low	low	low
Chen LY 2021	low	unclear	unclear	unclear	low	low	low	high
Chen R 2015	high	unclear	unclear	unclear	low	low	low	low
Chen YF 2009	unclear	unclear	unclear	unclear	low	low	low	low
Chen ZC 2014	low	unclear	unclear	unclear	low	low	low	high
Cheng ZL 2016	unclear	unclear	unclear	unclear	low	low	low	low
Cui YM 2014	unclear	unclear	unclear	unclear	low	low	low	low
Dai YP 2008	unclear	unclear	unclear	unclear	low	low	low	low
Du PK 2016	unclear	unclear	unclear	unclear	low	low	low	low
Du XL 2010	high	unclear	unclear	unclear	low	low	low	low
Feng JW 2017	low	unclear	unclear	unclear	low	low	low	high
Gao YD 2011	unclear	unclear	unclear	unclear	low	low	low	low
Ge J 2013	unclear	unclear	unclear	unclear	low	low	low	low
Guo WJ 2013	unclear	unclear	unclear	unclear	low	low	low	low
He J 2010	unclear	unclear	unclear	unclear	low	low	low	low
He JQ 2013	unclear	unclear	unclear	unclear	low	low	low	low
He XY 2006	unclear	unclear	unclear	unclear	low	low	low	low
Hua GC 2002	unclear	unclear	unclear	unclear	low	low	low	low
Huang DL 2009	high	unclear	unclear	unclear	low	low	low	low
Huang JL 2010	low	unclear	unclear	unclear	low	low	low	high
Huang M 2004	unclear	unclear	unclear	unclear	low	low	low	low
Huang XZ 2014	high	unclear	unclear	unclear	low	low	low	low
Ji DY 2014	unclear	unclear	unclear	unclear	low	low	low	low
Jia HB 2008	unclear	unclear	unclear	unclear	low	low	low	low
Jia HY 2021	unclear	unclear	unclear	unclear	low	low	low	low
Jiang BN 2009	unclear	unclear	unclear	unclear	low	low	low	low
Jiao XL 2008	unclear	unclear	unclear	unclear	low	low	low	low
Kou XF 2012	high	unclear	unclear	unclear	low	low	low	low
Lei GR 2014	unclear	unclear	unclear	unclear	low	low	low	low

TABLE 2 Quality assessment of the included studies using the Cochrane risk of bias (ROB) assessment tool^a.

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall quality
Li JH 2008	unclear	unclear	unclear	unclear	low	low	low	low
Li SJ 2014	high	unclear	unclear	unclear	low	low	low	low
Li XF 2014	high	unclear	unclear	unclear	low	low	low	low
Li XH 2011	unclear	unclear	unclear	unclear	low	low	low	low
Li XJ 2010	unclear	unclear	unclear	unclear	low	low	low	low
Li XL 2023	low	unclear	unclear	unclear	low	low	low	high
Li XR 2011	unclear	unclear	unclear	unclear	low	low	low	low
Li YJ 2018	low	unclear	unclear	unclear	low	low	low	high
Li ZY 2013	high	unclear	unclear	unclear	low	low	low	low
Lin YQ 2006	unclear	unclear	unclear	unclear	low	low	low	low
Ling YX 2006	unclear	unclear	unclear	unclear	low	low	low	low
Liu JX 2004	unclear	unclear	unclear	unclear	low	low	low	low
Liu JX 2010	unclear	unclear	unclear	unclear	low	low	low	low
Liu MF 2009	unclear	unclear	unclear	unclear	low	high	low	low
Liu S 2004	high	unclear	unclear	unclear	low	low	low	low
Liu XH 2013	unclear	unclear	unclear	unclear	low	low	low	low
Liu XJ 2008	unclear	unclear	unclear	unclear	low	low	low	low
Liu XY 2016	low	unclear	unclear	unclear	low	low	low	high
Liu Y 2003	unclear	unclear	unclear	unclear	low	high	low	low
Ma YX 2016	unclear	unclear	unclear	unclear	low	low	low	low
Mai Y 2005	unclear	unclear	unclear	unclear	low	high	low	low
Nie XP 2020	unclear	unclear	unclear	unclear	low	low	low	low
Peng J 2021	low	unclear	unclear	unclear	low	low	low	high
Qin DY 2014	unclear	unclear	unclear	unclear	low	low	low	low
Qin QA 2013	unclear	unclear	unclear	unclear	low	low	low	low
Ren JM 2006	unclear	unclear	unclear	unclear	low	low	low	low
Shang S 2014	unclear	unclear	unclear	unclear	low	low	low	low
Shen DD 2017	low	unclear	unclear	unclear	low	low	low	high
Shi JP 2008	unclear	unclear	unclear	unclear	low	low	low	low
Su HM 2007	unclear	unclear	unclear	unclear	low	low	low	low
Sun BJ 2014	unclear	unclear	unclear	unclear	low	low	low	low
Sun HY 2005	high	unclear	unclear	unclear	low	low	low	low
Sun T 2019	unclear	unclear	unclear	unclear	low	low	low	low
Tai SEGL 2011	unclear	unclear	unclear	unclear	low	high	low	low
Tian ZC 2008	unclear	unclear	unclear	unclear	low	low	low	low

TABLE 2 (Continued) Quality assessment of the included studies using the Cochrane risk of bias (ROB) assessment tool^a.

Blinding of participants and Author, Other Random Allocation Blinding of Incomplete Selective sequence generation concealment outcome reporting bias quality year data personnel Wang DH low unclear unclear unclear low low low high 2023 Wang HL unclear unclear unclear unclear low low low low 2013 Wang HR low unclear unclear unclear low low low high 2010 Wang JF 2018 unclear unclear unclear unclear low low low low Wang MS unclear unclear unclear unclear low low low low 2012 Wang QY high unclear unclear unclear low high low low 2012 unclear Wang SW unclear unclear unclear low low low low 2014 Wang WH unclear unclear unclear unclear low low low low 2006 unclear unclear unclear Wang XH high low low low low 2015 high Wu I 2011 low unclear unclear unclear low low low Wu XJ 2006 unclear unclear unclear unclear low low low low Wu Y 2011 unclear unclear unclear unclear low low high low Wu ZX 2004 unclear unclear unclear unclear low low low low Xiao DF 2022 low unclear unclear unclear low low low high Xie RP 2010 unclear unclear unclear unclear low low low low Xie YQ 2004 unclear unclear unclear unclear low low low low Xin FB 2005 unclear unclear unclear unclear low low low low Xiong SC unclear unclear unclear unclear low low low low 2011 Xu CY 2012 unclear unclear unclear unclear low low low low Xu L 2008 unclear unclear unclear unclear low low low low Xu PF 2011 unclear unclear unclear unclear low low low low Xue JY 2013 unclear unclear unclear unclear low low low low Yan TQ 2016 unclear unclear unclear unclear low low low low Yan XY 2010 high unclear unclear unclear low low low low Yang JH 2010 low unclear unclear unclear low low low high Yang M 2009 unclear unclear unclear unclear low low low low Yang XW unclear unclear unclear unclear low low low low 2006 Yin HX 2004 unclear unclear unclear unclear low low low low Yin ZL 2020 low unclear unclear unclear low low low high Yu BQ 2003 high unclear unclear unclear low low low low Zang ZX 2010 unclear unclear unclear unclear high high low low

TABLE 2 (Continued) Quality assessment of the included studies using the Cochrane risk of bias (ROB) assessment tool^a.

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall quality
Zhang GJ 2010	unclear	unclear	unclear	unclear	low	low	low	low
Zhang H 2009	high	unclear	unclear	unclear	high	low	low	low
Zhang HM 2004	high	unclear	unclear	unclear	high	low	low	low
Zhang HX 2006	unclear	unclear	unclear	unclear	low	low	low	low
Zhang L 2007	unclear	unclear	unclear	unclear	low	low	low	low
Zhang L 2010	unclear	unclear	unclear	unclear	low	high	low	low
Zhang MX 2018	unclear	unclear	unclear	unclear	low	low	low	low
Zhang RL 2008	unclear	unclear	unclear	unclear	low	high	low	low
Zhang XK 2017	unclear	unclear	unclear	unclear	low	low	low	low
Zhang XZ 2018	unclear	unclear	unclear	unclear	low	low	low	low
Zhang YP 2004	high	unclear	unclear	unclear	low	low	low	low
Zhao YX 2015	unclear	unclear	unclear	unclear	low	low	low	low
Zheng YZ 2014	unclear	unclear	unclear	unclear	low	low	low	low
Zhu L 2014	unclear	unclear	unclear	unclear	low	low	low	low
Zhu XJ 2013	unclear	unclear	unclear	unclear	low	low	low	low
Zhuang JS 2004	unclear	unclear	unclear	unclear	low	low	low	low
Zi XH 2004	high	unclear	unclear	unclear	low	low	low	low

TABLE 2 (Continued) Quality assessment of the included studies using the Cochrane risk of bias (ROB) assessment tool^a.

^aHiggins, J.P.T., Green, S., 2011. Cochrane Handbook for Systematic Reviews of Interventions. London, The Cochrane Collaboration.





3.5.2.2 SXNI plus CTs vs. CTs plus other injections

Seven studies involving 897 participants evaluated ADL by the BI. Due to significant heterogeneity ($I^2 = 89\%$, p < 0.05), a random effects model was used. The results showed that SXNI plus CTs was

superior to CTs plus other injections for increasing BI scores (*MD*: 5.43, 95% *CI*: 0.48–10.39, Z = 2.15, p < 0.05) (Figure 6B). Sensitivity analysis by adjusting the statistical models showed that the metaanalysis results were robust (Supplementary Table S1). However, the difference in the BI scores between SXNI plus CTs and CTs plus other injections was not significant when five studies were removed one at a time (Chen, 2021; Li, 2014; Ma, 2016; Zhang et al., 2009; Zhao, 2015) (Supplementary Figure S16). Mixed-effect metaregression did not reveal sample size, mean age, total dose of SXNI, publication year, or quality of studies as sources of heterogeneity (Supplementary Table S1).

3.6 AEs

Seventy-one studies reported AEs, and 49 reported no AEs. Twenty-two studies reported AEs related to the SXNI group or non-SXNI group, five of which did not report the number of AEs in the SXNI group, and two did not report the number of AEs in the non-SXNI group. SXNI plus CTs (1.53%, 61/3,994) was similarly safe to CTs alone or CTs plus other injections (1.32%, 50/3,797). The most common AEs related to SXNI were cardiovascular system events, and the five most common symptoms were dizziness, flushing, palpitations, nausea, and headache. The most common AEs related to the non-SXNI group were digestive system events, and the five most common symptoms were palpitations, nausea, dizziness, flushing, and vomiting. Moreover, all these symptoms in both the SXNI group and the non-SXNI group were mild and disappeared after discontinuation of the drug and symptomatic treatment. The symptoms of AEs are detailed in Supplementary Table S3.

3.7 Quality of evidence

We used the GRADE tool to systematically evaluate the quality of each outcome. The levels of evidence for CER and BI scores were low in SXNI plus CTs compared with CTs alone for AIS, while the levels of evidence for the NIHSS score and CSS score were very low (Table 3). Additionally, the level of evidence for the CER, NIHSS, CSS, and BI scores were all very low for SXNI plus CTs compared with CTs plus other injections for AIS (Table 3). The grade was decreased mainly because of the low methodological quality of the included studies, high heterogeneity among the included studies, and potential publication bias.

4 Discussion

4.1 Summary of the evidence

A total of 116 studies involving 12,401 participants were included in this review to assess the efficacy and safety of SXNI as an add-on therapy for patients with AIS. The meta-analysis results showed that SXNI plus CTs was superior to CTs alone or CTs plus other injections in improving patients' CER, NIHSS, CSS, and BI scores, suggesting that SXNI combined with CTs can significantly improve clinical efficacy, reduce neurological deficits,



and promote the recovery of ADL in patients with AIS. Subgroup analysis and mixed-effect meta-regression analysis indicated that duration of intervention, daily dose of SXNI, total dose of SXNI, sample size, mean age, different injections used in the control group, quality of studies, and publication year were not sources of heterogeneity. Except for the BI score between SXNI plus CTs and CTs plus other injections, the sensitivity analysis of the remaining indicators demonstrated that the meta-analysis results were robust. Sensitivity analysis revealed that the difference in BI scores between SXNI plus CTs and CTs plus other injections was not significant when five studies were removed one at a time (Chen, 2021; Li, 2014; Ma, 2016; Zhang et al., 2009; Zhao, 2015). In terms of safety, based on the results of this study, we cautiously believe that SXNI is relatively safe and reliable. Publication bias was found in the CER and NIHSS scores. Only 15 (12.9%) studies were judged to be of moderate to high quality. The levels of evidence for the CER, NIHSS, CSS, and BI scores were very low to low quality. Therefore, the results of this study should be considered with caution.

According to traditional Chinese medicine theory, the main pathological changes in AIS are qi deficiency and blood stasis. Qi is regarded as the main material basement that constitutes the human body and maintains life activities and an energy which manifests simultaneously on the physical and emotional-mental-spiritual level, and it has functions of promoting, warming, defense, transformative action and containment) (Jiang et al., 2023; Tian et al., 2024). Therefore, clinical treatment of this disease is mainly carried out by supplementing qi, promoting blood circulation, and dredging meridians and collaterals. SXNI is an extract of G. biloba leaves that promotes blood circulation, eliminates blood stasis, unblocks meridians, tonifies qi, and strengthens the brain (Ding, 2018; Zhang, 2019). From the perspective of Western medicine, SXNI can improve blood rheology, inhibit platelet aggregation, and reduce blood viscosity (Zhang et al., 2005). Ginkgolides can inhibit glutamate receptor-gated calcium channels, significantly reduce Ca²⁺ content in brain cells, prevent intracellular Ca²⁺ overload, and reduce cascade reaction-induced brain cell necrosis (Chandrasekaran et al., 2001). SXNI can improve the energy

$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Study		Mean SD			ntrol SD	Mean Difference	MD	95%-CI	Weight (common)		
Kou XF 2012 50 3.44 13.8 50 52.20 5 -1.76 -2.44 -1.06 -2.46	Du XL 2010	99	7.83 4.56	99	14.75	7.97 -		-6.92	[-8.73; -5.11]	0.7%	7.9	
LiX 2023 35 7.21 1.13 83 13.47 1.66 +							+				9.2	
Li V) 2018 62 5.18 102 62 9.78 1.18 6 Peng J 2021 73 7 3.58 114 57 6.11 135 Shen DD 2017 75 6.05 112 57 9.16 1.65 Shen DD 2017 75 6.05 112 57 9.16 1.65 Shen DD 2017 75 6.05 112 57 9.16 1.65 Shen DD 2017 75 6.05 114 64 13.25 $+$ $ -$											9.2	
Peng 2 2021 s7 33 33 141 37 6.11 135 Shen D2 2023 63 126 57 94 18 165 Wang DF 2023 63 0.52 0.58 126 57 94 18 18 55 Wang DF 2023 64 26 57 44 18 18 354 $+$ $-2.58 [-3.69, -2.50]$ 8.5% Common effect model 48 8.05 1.14 48 14.33 2.26 $+$ $-3.61 [-1.26, -0.33]$ 47.2% Shar D2 2012 64 8.65 1.14 48 14.33 2.26 $+$ $-3.61 [-1.26, -0.33]$ 47.2% Shar D2 2013 64 8.805 1.14 48 14.33 2.26 $+$ $-3.61 [-1.26, -0.33]$ 42.5% Common effect model 563 563 563 563 563 563 563 563 563 563											9.3 9.4	
Shen DD 2017 Wang DH 2023 Wang DH 2023 Wang DH 2023 Wang DH 2023 Wang DH 2024 Wang DH 2024 Wang DH 2024 Wang DH 2024 Wang DH 2024 Wang DH 2024 Wang DH 2024 Style To stal Sector Experimental Control Sudy Total Mans SD Total Mans DS Total Mans SD Total Mans SD Common effect model DP 2016 40 313 110 Control Sudy Total Mans SD Total Mans DD Control Carbon effect model DP 2016 40 313 110 Control Sudy Total Mans SD Total Mans DD Control Carbon effect model DP 2016 40 313 110 Control Carbon effect model DP 2016 40 313 110 Control Carbon effect model DD 2017 Control Carbon effect model DD 2017 Control Carbon effect model DD 2017 Control DD 2017 Control Con											9.3	
Wang DH 2023 40 352 0.58 0.43 0.61 -0.68 -1.05 -0.68 -1.25 -0.68 -1.25 -0.68 -1.25 -0.68 -1.25 -0.68 -1.25 -0.68 -1.25 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -0.68 -2.26 -2.27							÷ .				9.3	
Yin Zi, 2020 34 7.55 1.14 34 10.25 1.74 44.5% Common effect model Heterogeneity, $f^2 = 93\%$, $f^2 = 4.0898$, $p < 0.01$ 6-30 -2.80 <	Wang DH 2023	60	3.52 0.58	60	4.36	0.61		-0.84	[-1.05; -0.63]	47.2%	9.5	
Zhang XZ 2018 48 8.05 1.14 48 14.33 2.26 + -5 6.28 [-7.00, -5.66] 4.2% Common effect model Hetrogenety, f = 05%, c = 4.268, p < 0.01											8.5	
Common effect model 563 563 Feedback Sectors Model Weight Part 1988, $\tau^{+} = 0.01$ 5 SXMI plus CTs vs CTs alone: CSS accors Sudy Total Mean SD Total Mean SD Total Mean SD Total Mean Difference Model Telescopenity, $\tau^{+} = 0.86, \rho = 0.01$ Common effect model 561 Sectors 100.0%, $\tau^{-} = 0.01$ Common effect model 101 Sectors 100.00 Sectors 100.0%, $\tau^{-} = 0.01$ Common effect model 101 Sectors 100.00 Sectors 100.0%, $\tau^{-} = 0.01$ Common effect model 101 Sectors 100.00 Sectors 100.0							_ T				9.2 9.2	
Random effects model Heterogeneity: <i>F</i> = 99%, <i>f</i> = 4.088, <i>p</i> < 0.01 -4.00 [-5.22; -2.78]			0.00 1.11		11.00	2.20			1		0.2	
B. SXNI plus CTs vs CTs alone: CSS score Study Total Meen SD Total Meen SD Meen Difference MD Pays-CI (common) Di PK 2016 49 3.0 3.19 124 69 5.54 167 Gev D2 014 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 3.0 2.10 42 1450 360 49 49 40 2.11 20 111 20 111 20 112 40 16.0 60 25.70 3.30 40 44 40 40 2.00 30 5.00 3.00 40 450 30 5.00 3.00 40 450 30 5.00 3.00 40 450 30 5.00 3.10 40 450 40 40 2.00 30 5.00 3.00 40 450 30 5.00 3.10 40 450 40 40 2.00 30 5.00 3.00 40 450 30 5.00 3.10 40 450 40 40 2.00 40 40 2.00 30 5.00 3.00 40 40 2.00 30 50 0.00 40 40 2.00 40 40 40 2.00 40 40 40 2.00 40 40 40 2.00 40 40 40 2.00 40 40 40 2.00 41 40 4	Random effects mode	el	398, p < 0.01				–				100.0	
Experimental Control Mean 3D	SXNI plus CTs vs C	CTs alor	ne: CSS sc	ore			-5 0 5					
DUPK 2016 49 3.13 1.19 49 5.34 1.87 Gev 7D 2011 60 14.76 1.24 60 1569 1.03 LiX 2011 120 11.19 125 120 16.95 128 LiX 2011 59 120 1639 128 Wang HR 2015 53 108 3.90 35 1530 4.80 Yang HR 2010 53 1080 3.80 35 1530 4.80 Yang HR 2010 53 1080 3.80 35 1530 4.80 Yang HR 2010 53 1080 3.80 35 1530 4.80 Common effect model 591 Random effect model 591 Study Total Man SD Total Mean SD Man Difference MD 95%-C1 (common) 16.28 Yang HL 2013 40 661 128 40 7.38 13.0 Heterogeneity: $f^2 = 84\%$, $f^2 = 1.586$, $p < 0.01$ Heterogeneity: $f^2 = 84\%$, $f^2 = 1.586$, $p < 0.01$ Heterogeneity: $f^2 = 84\%$, $f^2 = 1.1586$, $p < 0.01$ Common effect model 217 Random effect model 217 Random effect model 217 Kudy Total Mean SD Total Mean SD Man Difference MD 95%-C1 (common) (1.52% 1.19) 5.25% Common effect model 217 Random effect model 217 Random 142 10 11 31 120 128 6.42 9 Study Total Mean SD Total Mean SD Man Difference MD 95%-C1 (common) (1.52% 1.19) 5.25% Common effect model 217 Random 141 118 120 11.19 128 6.42 9 Yang YK 2014 31 2.05 2.11 30 16.90 2.30 Control Cher LY 2021 35 326 2.11 30 16.90 12.80 6.22 Common effect model 217 Random 141 119 120 110 30 1180 0.24 10 7.30 13.0 LiX 2010 128 6.80 4.20 30 15.00 3.00 Cher LY 2013 30 9.65 2.11 30 16.90 3.00 Cher LY 2013 30 9.65 2.11 30 16.90 3.00 Cher LY 2013 40 6.91 12.80 6.82 9 Common effect model 217 Random effect model		Ex	perimental				Mean Difference	MD	95%-0			
$ \begin{array}{c} Gao VD 2011 & 60 14.76 1.24 & 60 15.69 1.03 \\ Li XF 2014 & 48 9.30 2.30 & 42 14.50 3.60 \\ Li XR 2011 & 90 12.40 1.66 60 52.70 3.3 \\ Mar X 2005 & 34 9.20 6.40 & 30 15.60 7.20 \\ Mar X 2015 & 34 9.20 6.40 & 30 15.60 7.20 \\ Mar X 2015 & 34 9.20 6.40 & 30 15.60 7.20 \\ Mar X 2015 & 34 9.20 6.40 & 30 15.60 7.20 \\ Mar X 2015 & 34 9.20 6.40 & 30 15.60 7.20 \\ Xang RL 2008 & 67 9.10 6.30 62 15.80 7.10 \\ Heterogeneity: f^{*} 95%, c^{*} 15.566, p < 0.01 \\ Heterogeneity: f^{*} 95%, c^{*} 15.566, p < 0.01 \\ C. SXNI plus CTs vs CTs plus other injections: NHS5 Secret \\ Study Total Mar SD Total Mean SD Mar Mar SD Total Mean SD Mar Mar Mar Mar Mar Mar Mar Mar Mar Mar$											10.7	
Li XF 2014 120 11 20 11 19 125 120 10 16 95 128 $-5.00 + -5.20 - 6.40 - 5.541 + 45.3\%$ Li XF 2011 20 11 90 12.40 160 60 2570 3.30 + $-5.70 - 6.08 - 5.44 + 45.3\%$ Li XF 2015 30 4.00 2.00 30 500 3.00 $6.10 - 7.30 - 4.10 + 6.20 - 2.20 + 2.8\%$ Comon offset model 581 530 4.80 $-5.00 + 10.50 - 7.00 + 10.50 + 2.50 + 10.50 - 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.50 + 7.10 + 5 + 5 + 1.50 + 2.26 + 1.21 + 2.26 + 2.2 +5 + 1.0 + 5 + 1.50 + 2.26 + 1.21 + 2.26 + 2.2 +5 + 1.0 + 2.26 + 1.21 + 2.26 + 2.2 +5 + 1.0 + 2.26 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.26 + 2.2 +5 + 1.21 + 2.27 + 2.28 + 1.10 + 2.28 +1.64 + 2.26 + 1.24 + -7.21 + 2.28 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + 2.2 + 2.25 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + 2.2 +1.64 + 2.26 + -2.26 + 2.4 + 2.4 + 2.4 + -2.26 + 2.4 + 2.4 + -2.26 + 2.4 + 2.4 + -2.26 + 2.4 + -2.4 + 2.4 + -2.4 + -2.4 + 2.4 + -2.4 + -2.4 + -2.4 + 2.4 + -2.4 + $											10.7	
LiXR 2011 90 1240 160 60 2570 330 +								-5.20	[-6.47; -3.93]	2.9%	10.4	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $											10.7	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $											10.6	
Wang HR 2010 53 10.63 50 15.30 6.30 6.43 9.36 Common effect model 581 536 536 536 67 9.10 6.30 62 15.80 7.10 -5.01 -7.27 1.96 0.2% Common effect model 581 536 536 536 -5.01 -7.38 -2.66 -7.27 1.96 0.2% Study Total Mean SD Total Mean SD Maan Difference -5.01 -7.38 -2.65 100.0% Sunt 2019 20 4.20 1.20 6.10 1.20 -3.01 -3.66 -5.72 1.23 4.06 Sunt 2019 20 4.20 1.20 6.12 -7.56 -7.37 1.96 -3.56 -6.57 -1.38 -0.57 -1.31 -0.95 -1.64 -2.20 2 4.06 -3.56 -6.57 -1.64 -2.20 2 4.66 -7.56 -7.56											10.4	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		53	10.60 3.50						[-7.30; -4.10]	1.8%	10.2	
Common effect model Heterogeneity: $t^2 = 93\%$, $t^2 = 13.6666$, $p < 0.01$ 5xtNI plus CTs vs CTs plus other injections: NIHSS score 5tudy Total Mean D5 Total Mean SD Mean Difference Muse Difference Study Chen LY 2021 35 326 211 36 227 143 40% 3 30 8 907 10 9 5126 2143 9 55%-C1 (common) (5 5%, 2 10, 1 20 6 10 1 20 1	Xie YQ 2004	30	13.65 8.87	30	16.31 9	.35		-2.66	[-7.27; 1.95]	0.2%	7.6	
Random effects model Heterogeneity: $l^2 = 99\%$, $t^2 = 13.6666$, $p < 0.01$ -5.01 [-7.38; -2.65] -5.01 [-7.38; -2.65]			9.10 6.30		15.80 7	.10					9.7	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Random effects mode	el	666 p < 0.01	536			–				100.0	
Experimental Control Mean Difference MD Weight 95%-Cl (common) Chen LY 2021 35 3.26 2.11 35 6.27 1.43			1 - 1									
Chen LY 2021 35 3.26 2.11 35 6.27 1.43 -3.01 -3.85 -2.17 23.9% Sun T 2019 20 4.20 21.02 0.61 1.24 40 7.36 1.31 -3.01 -3.65 -5.75 -1.43 4.0% Wang HL 2013 40 6.61 1.24 40 7.36 1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.31 -0.75 -1.32 2.5% Common effect model 217 217 217	SXNI plus CTs vs C			ectio			core			Weight	Weigh	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Study	Total	Mean SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(common)	random	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $											24.6	
Wang HL 2013 40 6.61 1.24 40 7.36 1.31 -0.75 -0.31 -0.75 -0.31 -0.75											14.69	
Zhao YX 2015 42 15.72 5.82 42 19.26 6.42 -3.54 [-6.16; -0.92] 2.5% Common effect model Heterogeneity: $l^2 = 84\%$, $z^2 = 1.1586$, $p < 0.01$ 217 217							1.				26.7	
Random effects model Heterogeneity: I ² = 84%, x ² = 1.1586, p < 0.01											11.29	
Heterogeneity: $l^2 = 84\%$, $t^2 = 1.1586$, $p < 0.01$ -6 -2 4 6 SXNI plus CTs vs CTs plus other injections: CSS score Study Total Mean SD Total Mean SD Weight Juit J 2010 28 Study Weight Li XJ 2010 28 Study Weight Li XJ 2010 28 Study Weight Li XJ 2010 28 Study Weight Via 2004 30 916.0 Colspan="2">Colspan="2" Colspan="2" <th col<="" td=""><td>Common effect mode</td><td>al 217</td><td></td><td>217</td><td></td><td></td><td>•</td><td>-1.64</td><td>[-2.06; -1.23]</td><td>100.0%</td><td>-</td></th>	<td>Common effect mode</td> <td>al 217</td> <td></td> <td>217</td> <td></td> <td></td> <td>•</td> <td>-1.64</td> <td>[-2.06; -1.23]</td> <td>100.0%</td> <td>-</td>	Common effect mode	al 217		217			•	-1.64	[-2.06; -1.23]	100.0%	-
SXNI plus CTs vs CTs plus other injections: CSS score Study Experimental Total Mean Control ND Mean Difference MD 95%-Cl (common) Li XJ 2010 28 8.50 4.20 30 15.40 3.20 -6.90 [-8.83:-4.97] 0.7% Huang M 2004 30 9.13 4.29 30 13.20 -6.90 [-8.83:-4.97] 0.7% Yua 2004 30 9.06 2.11 30 16.60 2.8 -6.30 [-5.63:-6.50] 1.9% Wang SW 2014 13 12.05 2.13 31 16.60 2.24 -9.48 -11.24:-7.72 0.8% Wang SW 2014 40 12.80 1.70 40 14.50 2.00 -7.52 [-7.09: -3.95] 1.0% Wang SW 2014 40 12.80 1.0 40 15.43 -7.32 [-8.81: -6.83] 1.1% King SC 2011 40 10.40 2.50 2.30			586, p < 0.01			г		-2.28	[-3.41; -1.16]		100.05	
Study Experimental Total Mean Control BD Mean Difference MD Weight 95%-Cl (common) Li XJ 2010 28 8.50 4.20 30 15.40 3.20 - - -6.90 [-8.83; -4.97] 0.7% Huang M 2004 30 9.13 4.29 30 13.20 - - -6.90 [-8.83; -4.97] 0.7% Wang SW 2014 31 12.20 1.10 30 16.60 2.88 - -6.73 [-6.76; -4.50] 1.9% Wang SW 2014 31 12.05 2.13 31 15.60 2.24 - -9.46 [-11.24; -7.72] 0.8% Wang QY 2012 40 12.80 7.07 40 14.50 2.00 - -7.32 [-8.81; -5.83] 1.1% Xiong SC 2011 40 10.83 2.10 40 18.15 4.32 - -7.32 [-8.81; -5.83] 1.1% Zhang MX 2018 40 2.120 1.0 40 2.50 2.30								6				
Li X J 2010 28 8.50 4.20 30 15.40 3.20 +		E	xperimental		Co	ontrol						
Huang M. 2004 30 9.13 4.29 30 13.32 4.84							Mean Difference					
Xu L 2008 30 9.06 2.11 30 14.69 2.35 -5.63 -6.76:-4.60 1.9% Wang SW 2014 33 12.20 1.0 30 16.00 0.80 610 15.62: 6.81 10.6% Wang SW 2011 33 12.25 2.13 31 15.60 2.24 -3.55 [-4.62:-2.48] 2.1% Chen R 2015 39 8.14 3.67 39 7.62 4.25 -9.46 [-1.24:-7.72] 0.8% Xiong SC 2011 40 12.80 1.70 40 14.50 2.00 -7.32 -7.89 3.7% Xiong SC 2011 40 14.80 1.53 2.4 -7.32 -8.81: -5.83 1.1% Zhang MX 2018 40 2.20 10 40 2.50 2.30 -7.71 -8.31: -3.31 3.9% Shi JP 2008 41 12.25 3.3 17.56 6.87 -7.31 -7.31: -3.11 0.4% UJH 2008 41 12.26 1.68 <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>+</td> <td></td> <td></td> <td></td> <td>3.0 2.9</td>							+				3.0 2.9	
Wang SW 2014 31 22.10 1.10 30 16.00 0.80							-				3.1	
Chen R 2015 39 8.14 3.67 39 17.62 4.25 + -9.46 [-11.24],-7.72] 0.8% Wang QY 2012 40 12.80 1.70 40 14.84 3.68 + -5.52 7.709 -3.991 1.0% Xiong SC 2011 40 12.80 1.70 40 14.50 2.00 + -7.32 -8.81 -5.83 1.1% Zhang MX 2018 40 21.20 1.10 40 25.30 2.30 + -7.32 -8.81 -8.83 1.1% Shi JP 2006 41 12.25 1.30 41 7.56 6.87 - -5.06 -5.79 -3.31 3.9% Ki JP 2008 44 14.20 1.88 - -2.04 [-2.44], -1.24] 3.8% Che YQ 2005 46 9.60 2.80 44 10.20 6.80 -0.30 [-2.35], -2.03] 3.7% Jiang BN 2009 55 1.80 0.05 51.23.69 1.05 4.467 9.37 -2.34 [-5.36], -7.25] 8.1% -2.34 [-5.36],											3.1	
Tian ZC 2008 66 6.32 2.13 24 11.84 3.68	Wu J 2011						*	-3.55	[-4.62; -2.48]		3.1	
Wang QY 2012 40 12.80 1.70 40 14.50 2.00 -1.70 [-2.51;-0.89] 3.7% Xiong SC 2011 40 10.83 2.10 40 18.15 4.32 + -7.32 [-8.11;-5.83] 1.1% Zhang MX 2018 40 21.20 1.10 40 25.30 2.30 + -7.32 [-8.11;-5.83] 1.1% Shi JP 2008 41 12.25 1.30 41 17.31 1.98 -5.06 [-5.79; -4.33] 4.7% Ma YX 2016 43 11.85 5.33 41 620 1.88 -5.06 -5.77 [-8.31; -3.11] 0.4% Li JH 2008 44 14.61 1.620 1.88 -2.04 -2.85; -2.25 0.4% Che YQ 2005 46 9.90 5.80 44 16.20 6.50 -0.30 [-2.85; -2.25] 0.4% Liu XY 2016 47 9.82 4.83 47 13.55 4.54 -3.33 [-5.85; -2.25] 0.4% Sum HY 2005 52 1.30 5.20 51 16.70 8.10 -640 [-9.03; -3.77] 0.4% Cao XM 2015 56 12.30 9.10 551 4.640 7.80 -3.70 [-6.16; -	Oh	39					+	-9.48	[-11.24; -7.72]	0.8%	3.0 3.0	
Xiong SC 2011 40 10.83 2.10 40 18.15 4.32 + -7.32 [-8.81]-5.83] 1.1% Zhang MX 2018 40 12.0 10 40 25.0 2.30 - - -7.32 [-8.81]-5.83] 1.1% Shi JP 2008 41 12.25 1.30 41 17.31 1.98 - -5.06 [-5.79]-4.33] 3.9% Ma YX 2016 43 11.85 5.33 43 17.56 6.87 - -5.71 [-8.31]-3.11] 0.4% Li JH 2008 44 14.61 1.96 44 16.20 1.88 -2.04 [-2.84]-1.24] 3.8% Che YQ 2005 46 9.80 5.80 44 10.20 6.50 -0.30 [-2.85]-2.25] 0.4% Liu XY 2016 47 9.62 4.81 47 13.55 4.54 -3.93 [-5.83]-7.02] 0.4% Wang XH 2015 51 8.40 0.20 51 16.67 9.37 - -2.31 [-5.76].1.14] 0.2% Cao XM 2015 56 51.04.67 9.30 - - -1.21 [-5.86].82.04% . . - -7.80	Chen R 2015	56					-				3.0	
Zhang MX 2018 40 21.20 1.10 40 25.30 2.30 -4.10 [-4.89]-3.31] 3.9% Shi JP 2008 41 12.25 13.0 41 7.31 1.98 -5.06 [-5.79]-4.33] 4.7% Ma YX 2016 43 11.85 5.33 43 17.56 6.87 -5.71 [-8.31]-3.11] 0.4% Li JH 2008 44 14.16 16 44 6.20 1.88 2.04 [-2.24]-1.21 3.8% Che VO 2005 46 9.90 5.80 44 10.20 6.50 -0.30 [-2.28]-2.25] 0.4% Liu XY 2016 47 9.62 483 47 15.54 3.93 [-5.83]-2.03] 0.7% Wang XH 2015 51 8.40 0.20 7.80 [-8.35]-7.25] 8.1% Jiang BN 2009 51 2.50 0.51 4.67	Chen R 2015 Tian ZC 2008					4.32	+	-7.32	[-8.81; -5.83]	1.1%	3.0	
Ma YX 2016 43 11.85 5.33 43 17.56 6.87 -5.71 [-3.31;-3.11] 0.4% Li JH 2008 44 14.16 196 44 16.20 188 -2.04 [-2.84;-1.24] 3.8% Che VO 2005 46 9.90 5.80 44 10.20 6.50 -2.04 [-2.84;-1.24] 3.8% Liu XY 2016 47 9.62 4.83 47 13.55 4.54 -3.03 [-2.84;-2.25] 0.4% Liu XY 2015 51 8.40 0.20 51 1.670 8.10 -6.40 [-3.35;-7.25] 8.1% Sun HY 2005 52 10.51 51 6.40 7.00 [-4.35;-7.25] 8.1% Cao XM 2015 56 12.00 5.10 56 4.64 7.00 -2.31 [-5.76; 1.14] 0.2% Zhang H2009 60 12.00 5.00 61 61.00 -3.70 [-6.16; -1.24] 0.4% Li JJ 2014 60 12.00 5.00 61 60 1.60	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011	40 40	12.80 1.70 10.83 2.10				a			3.9%	3.1	
Li JH 2008 44 14,16 196 44 16,20 1.88 -2.04 [-2.84;-1.24] 3.8% Che YQ 2005 46 9.90 50 44 10.20 6.50 -0.30 [-2.85; 2.25] 0.4% Liu XY 2016 47 9.62 4.83 47 13.55 4.54 -3.93 [-2.85; -2.25] 0.4% Wang XH 2015 51 8.40 0.20 51 16.70 8.10 -7.80 [-3.35; -7.25] 8.1% Sun HY 2005 52 10.30 5.0 16.70 8.10 -6.40 [-9.03; -3.77] 0.4% Zhang H 2009 60 12.70 5.60 85 16.47 7.80 -7.21 [-1.56; -1.62] 0.4% Li SJ 2014 60 12.80 5.06 616.50 7.90 -3.70 [-6.44; -1.24] 0.4% Jaing SEGL 2011 60 12.80 5.06 616.50 7.90 -3.70 [-6.44; -1.26] 0.4% Jaing SEGL 2011 60 12.80 5.06 616.50 7.90 -3.70 [-6.44; -1.26] 0.4% Zhang X 2010 65	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018	40 40 40	12.80 1.70 10.83 2.10 21.20 1.10	40	25.30		10				3.1	
Che YQ 2005 46 9.90 5.80 44 10.20 6.50	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008	40 40 40 41	12.801.7010.832.1021.201.1012.251.30	40 41	25.30 17.31	1.98		-5.06	[-5.79; -4.33]		2.8 3.1	
Liu XY 2016 47 9.62 4.83 47 13.55 4.54	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016	40 40 40 41 43	12.801.7010.832.1021.201.1012.251.3011.855.33	40 41 43	25.30 17.31 17.56	1.98 6.87		-5.06 -5.71	[-5.79; -4.33 [-8.31; -3.11]			
Sun HY 2005 52 10.30 5.20 51 16.70 8.10	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008	40 40 40 41 43 44	12.801.7010.832.1021.201.1012.251.3011.855.3314.161.96	40 41 43 44	25.30 17.31 17.56 16.20	1.98 6.87 1.88		-5.06 -5.71 -2.04	[-5.79; -4.33 [-8.31; -3.11 [-2.84; -1.24	3.8%	2.8	
Jiang BN 2009 55 12.36 9.10 55 14.67 9.37 2.31 [-5.76; 1.14] 0.2% Cao XM 2015 56 12.10 56 23.00 7.50 -11.20 [-1.368; -8.82] 0.4% Zhang H 2009 60 12.20 5.60 58 16.40 7.80 11.20 [-1.58; -8.82] 0.4% Li SJ 2014 60 12.80 5.50 60 16.60 7.90 3.70 [-6.14; -1.24] 0.4% Jia BE 2008 62 11.30 4.20 61 19.60 5.80 - -8.20 [-9.614; -1.24] 0.4% Zhang XK 2017 62 9.73 1.17 62 7.188 1.42 - -8.20 [-9.68; -6.82] 1.3% Zhang XK 2017 62 9.73 1.17 62 7.188 1.42 - -8.20 [-9.68; -6.82] 1.3% Zang ZX 2010 66 12.00 5.80 + - -8.20 [-9.68; -6.82] 1.3% Zhang YK 2017 62 9.73 1.76 7.188 1.42 - -8.16 [-6.61; -7.61] 0.4%	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016	40 40 41 43 44 46 47	12.80 1.70 10.83 2.10 21.20 1.10 12.25 1.30 11.85 5.33 14.16 1.96 9.90 5.80 9.62 4.83	40 41 43 44 44 47	25.30 17.31 17.56 16.20 10.20 13.55	1.98 6.87 1.88 6.50 4.54		-5.06 -5.71 -2.04 -0.30 -3.93	[-5.79; -4.33 [-8.31; -3.11] [-2.84; -1.24] [-2.85; 2.25] [-5.83; -2.03]	3.8% 0.4% 0.7%	3.0	
Cao XM 2015 56 10 66 23.30 7.50	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015	40 40 41 43 44 46 47 51	12.80 1.70 10.83 2.10 21.20 1.10 12.25 1.30 11.85 5.33 14.16 1.96 9.90 5.80 9.62 4.83 8.40 0.20	40 41 43 44 44 47 51	25.30 17.31 17.56 16.20 10.20 13.55 16.20	1.98 6.87 1.88 6.50 4.54 2.00		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80	[-5.79; -4.33] [-8.31; -3.11] [-2.84; -1.24] [-2.85; 2.25] [-5.83; -2.03] [-8.35; -7.25]	3.8% 0.4% 0.7% 8.1%	3.0 3.1	
Zhang H 2009 60 12 20 560 58 16 40 7.80 370 -616:-1.24 0.4% Li SJ 2014 60 12 80 50 60 16 50 7.90 370 -616:-1.24 0.4% Jai SEGL 2011 60 12 80 50 60 16 50 7.90 370 -616:-1.24 0.4% Jai HB 2008 62 11.30 4.20 61 19.50 3.60 - -8.20 [-9.68:-6.82] 1.3% Zhang XK 2016 65 22.00 2.22 62 2.710 5.91 4.35 [-6.61:-7.04] 0.4% Zhang XK 2010 66 12.00 5.80 - 5.67 [-8.58:-2.49] 0.4% Yu BQ 2003 66 7.73 8.42 75 13.40 10.80	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Sun HY 2005	40 40 41 43 44 46 47 51 52	$\begin{array}{ccccc} 12.80 & 1.70 \\ 10.83 & 2.10 \\ 21.20 & 1.10 \\ 12.25 & 1.30 \\ 11.85 & 5.33 \\ 14.16 & 1.96 \\ 9.90 & 5.80 \\ 9.62 & 4.83 \\ 8.40 & 0.20 \\ 10.30 & 5.20 \end{array}$	40 41 43 44 44 47 51 51	25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70	1.98 6.87 1.88 6.50 4.54 2.00 8.10		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40	[-5.79; -4.33 [-8.31; -3.11 [-2.84; -1.24 [-2.85; 2.25 [-5.83; -2.03 [-8.35; -7.25 [-9.03; -3.77]	3.8% 0.4% 0.7% 8.1% 0.4%	3.0 3.1 2.8	
Li SJ 2014 60 12.80 5.50 60 16.50 7.90	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Sun HY 2005 Jiang BN 2009	40 40 41 41 43 44 46 47 51 52 55	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	40 41 43 44 44 47 51 51 55	25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70 14.67	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31	[-5.79; -4.33 [-8.31; -3.11 [-2.84; -1.24 [-2.85; 2.25 [-5.83; -2.03 [-8.35; -7.25 [-9.03; -3.77 [-5.76; 1.14]	3.8% 0.4% 0.7% 8.1% 0.4% 0.2%	3.0 3.1 2.8 2.6	
Jia HB 2008 62 11.30 4.20 61 19.50 3.60 + -8.20 [-9.58; -56.82] 1.3% Zhang XK 2017 62 7.73 1.7 62 7.88 1.42 -8.15 [-9.68; -56.82] 1.3% Zang XK 2010 66 11.10 5.86 15.45 7.92 -4.35 [-9.68; -16.76] 11.8% Yu BO 2003 66 7.73 8.42 75 13.40 10.80 -5.67 [-9.68; -2.42] 0.2% Zhang HM 2004 74 11.60 5.80 7.16 0.74% -5.67 [-8.58; -2.49] 0.2% Zhang LV 2014 73 12.70 5.10 7.17.80 7.40 -5.10 [-7.16; -3.04] 0.6% Xin LB 2014 1.26 5.50 118 15.30 7.70 -0.01 [-0.59] [-3.70] -5.70 [-5.73] 8.2% 0.75 12 10.88 -5.70 -5.70 .74% 0.73 0.70% -5.70 .74% <td>Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Jiang BN 2009 Cao XM 2015 Zhang H 2009</td> <td>40 40 41 43 44 46 47 51 52 55 56 60</td> <td>12.80 1.70 10.83 2.10 21.20 1.10 12.25 1.30 11.85 5.33 14.16 1.96 9.90 5.80 9.62 4.83 8.40 0.20 10.30 5.20 12.36 9.10 12.10 5.10 12.70 5.60</td> <td>40 41 43 44 44 47 51 51 55 56 58</td> <td>25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70 14.67 23.30 16.40</td> <td>1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80</td> <td></td> <td>-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70</td> <td>[-5.79; -4.33] [-8.31; -3.11] [-2.84; -1.24] [-2.85; -2.25] [-5.83; -2.03] [-8.35; -7.25] [-9.03; -3.77] [-5.76; 1.14] [-13.58; -8.82] [-6.16; -1.24]</td> <td>3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4%</td> <td>3.0 3.1 2.8 2.6 2.9 2.9</td>	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Jiang BN 2009 Cao XM 2015 Zhang H 2009	40 40 41 43 44 46 47 51 52 55 56 60	12.80 1.70 10.83 2.10 21.20 1.10 12.25 1.30 11.85 5.33 14.16 1.96 9.90 5.80 9.62 4.83 8.40 0.20 10.30 5.20 12.36 9.10 12.10 5.10 12.70 5.60	40 41 43 44 44 47 51 51 55 56 58	25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70 14.67 23.30 16.40	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70	[-5.79; -4.33] [-8.31; -3.11] [-2.84; -1.24] [-2.85; -2.25] [-5.83; -2.03] [-8.35; -7.25] [-9.03; -3.77] [-5.76; 1.14] [-13.58; -8.82] [-6.16; -1.24]	3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4%	3.0 3.1 2.8 2.6 2.9 2.9	
Zhang XK 2017 62 9.73 1.17 62 17.88 1.42 ■ −8.15 [−8.61; −7.69] 11.8% Zhang YP 2004 66 11.10 5.86 58 5.792 −4.35 [−6.83; −1.87] 0.4% Zang ZX 2010 65 22.00 5.22 62 27.10 5.91 −5.10 [−7.04] -3.16 0.7% Yu BQ 2003 66 7.73 8.42 75 13.40 10.80 −5.67 [−8.65; −2.49] 0.2% Zhang JM 2004 66 5.10 73 17.80 7.40 −3.80 [−6.11; −1.49] 0.5% Zhu L 2014 73 12.00 5.10 73 17.80 7.40 −3.80 [−6.11; −1.49] 0.5% Yin HX 2004 95 12.06 5.00 14.55 0.98 −2.49 [−2.78] -2.01 2.85% Win HS 2004 95 12.06 5.00 16 16.30 7.70 </td <td>Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong XC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Vang XH 2015 Sun HY 2005 Jiang BN 2009 Cao XM 2015 Zhang H 2009 Li SJ 2014</td> <td>40 40 41 43 44 46 47 51 52 55 56 60 60 60</td> <td>$\begin{array}{llllllllllllllllllllllllllllllllllll$</td> <td>40 41 43 44 44 47 51 51 55 56 58 60</td> <td>25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70 14.67 23.30 16.40 16.50</td> <td>1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90</td> <td>• • •</td> <td>-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70</td> <td>$\begin{bmatrix} -5.79; -4.33\\ [-8.31; -3.11]\\ [-2.84; -1.24\\ [-2.85; 2.25]\\ [-5.83; -2.03]\\ [-8.35; -7.25]\\ [-9.03; -3.77]\\ [-5.76; 1.14\\ [-13.58; -8.822\\ [-6.16; -1.24]\\ [-6.14; -1.26] \end{bmatrix}$</td> <td>3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4% 0.4%</td> <td>3.0 3.1 2.8 2.6 2.9 2.9 2.9 2.9</td>	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong XC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Vang XH 2015 Sun HY 2005 Jiang BN 2009 Cao XM 2015 Zhang H 2009 Li SJ 2014	40 40 41 43 44 46 47 51 52 55 56 60 60 60	$\begin{array}{llllllllllllllllllllllllllllllllllll$	40 41 43 44 44 47 51 51 55 56 58 60	25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70 14.67 23.30 16.40 16.50	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90	• • •	-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70	$\begin{bmatrix} -5.79; -4.33\\ [-8.31; -3.11]\\ [-2.84; -1.24\\ [-2.85; 2.25]\\ [-5.83; -2.03]\\ [-8.35; -7.25]\\ [-9.03; -3.77]\\ [-5.76; 1.14\\ [-13.58; -8.822\\ [-6.16; -1.24]\\ [-6.14; -1.26] \end{bmatrix}$	3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4% 0.4%	3.0 3.1 2.8 2.6 2.9 2.9 2.9 2.9	
Zhang YP 2004 66 11.10 5.86 5.86 15.45 7.92 -+ -4.35 [-6.83; -1.87] 0.4% Zang ZX 2010 65 22.00 22.710 5.91 -+ -5.16 [-7.04; -3.16] 0.7% Yu BO 2003 66 7.73 8.42 75 13.40 10.80 -5.67 [-8.85; -2.49] 0.2% Zhang HM 2004 74 11.60 5.80 70 15.40 8.10 -3.80 [-6.11; -1.49] 0.5% Zhu L 2014 73 12.07 5.10 73 7.40 -+ -5.10 [-7.16; -3.04] 0.6% Yin HX 2004 95 12.06 1.06 90 14.55 9.8 -0.01 [-7.16; -3.20] 28.5% Sun BJ 2014 100 4.20 2.12 100 4.21 2.03 -0.01 [-0.59; 0.57] 7.4% Qin QA 2013 120 12.00 5.50 116 16.30	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Jiang BN 2009 Gao XM 2015 Zhang H 2009 Li SJ 2014 Tai SEGL 2011	40 40 41 41 43 44 46 47 51 52 55 55 56 60 60 60	$\begin{array}{llllllllllllllllllllllllllllllllllll$	40 41 43 44 44 47 51 55 56 58 60 60	25.30 17.31 17.56 16.20 13.55 16.20 14.67 23.30 16.40 16.50 19.60	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80	+ + + + + +	-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70 -10.70	$\begin{bmatrix} -5.79; -4.33\\ [-8.31; -3.11]\\ [-2.84; -1.24]\\ [-2.85; 2.25]\\ [-5.83; -2.03]\\ [-8.35; -7.25]\\ [-9.03; -3.77]\\ [-5.76; 1.14]\\ [-13.58; -8.82]\\ [-6.16; -1.24]\\ [-6.14; -1.26]\\ [-12.51; -8.89] \end{bmatrix}$	3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4%	3.0 3.1 2.8 2.6 2.9 2.9 2.9 2.9 3.0	
Zang ZX 2010 66 22.00 5.22 62 27.10 5.91	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiang SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Che YQ 2005 Liu XY 2016 Wang XH 2015 Sun HY 2005 Jiang BN 2009 Zhang H 2009 Li SJ 2014 Tai SEGL 2014 Tai SEGL 2014	40 40 40 41 43 44 46 47 51 52 55 56 60 60 60 60 62	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	40 41 43 44 44 47 51 55 56 58 60 60 60 61	25.30 17.31 17.56 16.20 13.55 16.20 14.67 23.30 16.40 16.50 19.60 19.50	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 3.60		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70 -10.70 -8.20	[-5.79; -4.33] [-8.31; -3.11] [-2.84; -1.24] [-2.85; 2.25] [-5.83; -2.03] [-8.35; -7.25] [-9.03; -3.77] [-5.76; 1.14] [-13.58; -8.82] [-6.16; -1.24] [-6.16; -1.24] [-6.14; -1.26] [-12.51; -8.89] [-12.51; -8.68]	3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.3% 1.3%	3.0 3.1 2.8 2.6 2.9 2.9 2.9 3.0 3.0 3.0	
Zhang HM 2004 74 11.60 5.80 70 15.40 8.10 3.80 [-6.11; -1.49] 0.5% Zhu L 2014 73 12.70 5.10 73 17.80 7.40	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Che YQ 2005 Liu XY 2016 Wang XH 2015 Zhang H 2009 Cao XM 2015 Zhang H 2009 Li SJ 2014 Tai SEGL 2014 Jia HB 2008 Zhang XK 2017 Zhang YZ 2004	40 40 41 43 44 46 47 51 55 55 56 60 60 60 60 60 62 62	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	40 41 43 44 44 47 51 55 56 58 60 60 60 61 62	25.30 17.31 17.56 16.20 13.55 16.20 16.70 14.67 23.30 16.40 16.50 19.60 19.50 17.88	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 3.60 1.42		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70 -3.70 -10.70 -8.20 -8.15 -4.35	[-5.79, -4.33] [-8.31, -3.11] [-2.84, -1.24] [-2.84, -1.24] [-2.85, 2.25] [-5.83, -2.03] [-8.35, -7.25] [-9.03, -3.77] [-5.76, 1.14] [-13.58, -8.82] [-13.58, -8.82] [-12.51, -8.89] [-9.58, -6.82] [-8.61, -7.69] [-6.83, -1.87]	3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4% 0.4% 0.4% 0.4% 1.3% 11.8%	3.0 3.1 2.8 2.6 2.9 2.9 2.9 3.0 3.0 3.0 3.1	
Zhu L 2014 73 12.70 5.10 73 17.80 7.40 -++ -5.10 [-7.16]<-3.04] 0.6% Yin HX 2004 95 12.06 10.06 90 14.55 0.98 -2.49 [-7.16]<-3.04]	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Zhang H 2009 Lis JL 2014 Tai SEGL 2011 Jia HB 2008 Zhang YP 2004 Zhang YP 2004 Zhang YP 2010	40 40 41 41 43 44 46 47 51 52 55 55 56 60 60 60 60 60 62 66 65	$\begin{array}{rrrr} 12.80 & 1.70 \\ 10.83 & 2.10 \\ 11.85 & 5.33 \\ 14.16 & 1.96 \\ 9.90 & 5.80 \\ 9.62 & 4.83 \\ 8.40 & 0.20 \\ 10.30 & 5.20 \\ 12.36 & 9.10 \\ 12.10 & 5.10 \\ 12.70 & 5.60 \\ 12.70 & 5.60 \\ 12.80 & 5.50 \\ 8.90 & 4.20 \\ 9.73 & 1.17 \\ 11.10 & 5.86 \\ 9.73 & 1.27 \\ 11.10 & 5.82 \\ 9.73 & 1.27 \\ 11.10 & 5.82 \\ 11.22.00 & 5.22 \\ 11.20 & 5.22 \\ $	40 41 43 44 47 51 55 56 58 60 60 61 62 58 62	25.30 17.31 17.56 16.20 10.20 13.55 16.20 14.67 23.30 16.40 16.50 19.60 19.50 19.50 17.88 15.45 27.10	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 3.60 1.42 7.92 5.91		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70 -10.70 -8.15 -4.35 -5.10	[-5.79, -4.33] [-8.31, -3.11] -2.84, -1.24] [-2.85, -2.25] [-5.83, -2.03] [-8.35, -7.25] [-9.03, -3.77] [-5.76, 1.14] [-13.58, -8.82] [-6.16; -1.24] [-6.16; -1.24] [-6.16; -1.24] [-12.51, -8.89] [-12.51, -8.682] [-9.58, -6.82] [-9.58, -6.82] [-9.58, -6.82] [-9.58, -6.82] [-9.58, -6.82] [-9.58, -6.82] [-7.04, -3.16] [-7.04, -3.16]	3.8% 0.4% 0.7% 8.1% 0.4% 0.4% 0.4% 0.4% 0.4% 1.3% 11.8% 0.4% 0.7%	3.0 3.1 2.8 2.9 2.9 2.9 3.0 3.0 3.0 3.1 2.9 3.0	
Yin HX 2004 95 12.06 1.06 90 14.55 0.98 -2.49 [-2.78; -2.20] 28.5% Sun BJ 2014 100 4.20 2.12 100 4.21 2.03 -0.01 [-0.59; 0.57] 7.4% Qin QA 2013 120 12.60 5.50 116 16.30 7.70 -3.70 [-5.41; -1.99] 0.8% Xin FB 2005 121 11.30 7.50 5.50 [-7.33; -3.70, 0.7%	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Vang XH 2015 Zhang H 2009 Cao XM 2015 Zhang H 2009 Cao XM 2015 Zhang H 2009 Li SJ 2014 Jia HB 2008 Zhang XK 2017 Zhang YP 2004 Zang ZX 2010 Yu BQ 2003	40 40 41 43 44 46 47 51 55 56 60 60 60 60 60 60 62 62 62 62 65 56	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	40 41 43 44 44 47 51 55 56 58 60 60 61 62 58 62 75	25.30 17.31 17.56 16.20 10.20 13.55 16.20 16.70 14.67 23.30 16.40 19.50 19.50 19.50 17.88 15.45 27.10 13.40	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.80 7.80 5.80 3.60 1.42 7.92 5.91 10.80		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -2.31 -11.20 -3.70 -3.70 -3.70 -3.70 -8.20 -8.20 -8.15 -4.35 -5.10 -5.67	[-5.79; -4.33] [-8.31; -3.11] [-2.84; -1.24] [-2.84; -1.24] [-2.85; 2.25] [-8.35; -7.25] [-8.35; -7.25] [-9.03; -3.77] [-5.76; 1.14] [-13.58; -8.82] [-6.14; -1.26] [-13.58; -6.82] [-6.14; -1.26] [-6.14; -1.26] [-6.14], -7.69] [-8.85; -2.49]	3.8% 0.4% 0.7% 8.1% 0.4% 0.4% 0.4% 0.4% 0.4% 1.3% 11.8% 0.4% 0.4% 0.7% 0.2%	3.0 3.1 2.8 2.6 2.9 2.9 2.9 3.0 3.0 3.0 3.1 2.9 3.0 2.7	
Sun BJ 2014 100 4.20 2.12 100 4.21 2.03 -0.01 [-0.59: 0.57] 7.4% Qin QA 2013 120 12.60 5.50 116 16.30 7.70 -3.70 [-5.41; -1.99] 0.8% Xin FB 2005 121 11.30 7.05 -1.510 [-7.33; -3.57] 0.7%	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Wang XH 2015 Zhang H 2009 Zhang H 2009 Zhang H 2009 Zhang KX 2017 Zhang YP 2004 Zhang XK 2017 Zhang YP 2004 Zhang XZ 2010 Yu BQ 2003 Zhang IM 2004	40 40 41 43 44 46 47 51 55 55 56 60 60 60 60 60 60 60 60 60 60 60 60 60	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	40 41 43 44 47 51 55 56 58 60 60 61 62 58 62 75 70	25.30 17.31 17.56 16.20 13.55 16.20 14.67 23.30 16.70 14.67 23.30 16.50 19.60 19.50 17.88 15.45 27.10 13.40 15.40	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 3.60 1.42 7.92 5.91 10.80 8.10		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70 -10.70 -8.20 -8.15 -4.35 -5.10 -5.67 -3.80	$\begin{bmatrix} -5.79, -4.33\\ -8.31, -3.11\\ -2.84, -1.24\\ -2.85, 2.25\\ -5.83, -2.03\\ -8.35, -7.25\\ -9.03, -3.77\\ -5.76, 1.14\\ -13.58, -8.82\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.16, -1.24\\ -6.11, -1.49\\$	3.8% 0.4% 0.7% 8.1% 0.4% 0.2% 0.4% 0.4% 0.4% 1.3% 11.8% 0.4% 0.4% 0.8% 0.5%	3.0 3.1 2.8 2.9 2.9 2.9 3.0 3.0 3.0 3.0 3.0 3.0 2.7 2.9	
Xin FB 2005 121 11.30 7.05 121 16.80 7.50 -5.50 [-7.33; -3.67] 0.7%	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Liu XY 2016 Wang XH 2015 Zhang H 2009 Cao XM 2015 Zhang H 2009 Zhang X 2014 Zhang XK 2017 Zhang XK 2017 Zhang XK 2017 Zhang XZ 2010 Yu GQ 2003 Zhang HM 2004	40 40 41 43 44 46 47 55 55 56 60 60 60 60 60 60 60 60 60 60 60 60 67 4 73	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	40 41 43 44 47 51 55 56 58 60 60 61 62 58 60 61 62 58 275 70 73	25.30 17.31 17.56 16.20 13.55 16.20 14.67 23.30 16.40 19.60 19.50 17.88 15.45 27.10 13.40 15.40 17.80	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 3.60 1.42 7.92 5.91 10.80 8.10 7.40		-5.06 -5.71 -2.04 -0.30 -3.93 -7.80 -2.31 -11.20 -3.70 -3.70 -8.20 -8.20 -8.15 -4.35 -5.10 -5.67 -3.80 -5.10	$\begin{bmatrix} -5.79, -4.33\\ -8.31, -3.11\\ -2.84, -1.24\\ -2.85, 2.25\\ -9.03, -3.77\\ -5.76, 1.14\\ -13.58, -7.85\\ -9.03, -3.77\\ -5.76, 1.14\\ -13.58, -8.82\\ -6.16, -1.24\\ -6.14, -1.26\\ -1.2, -5.8, -6.82\\ -8.61, -7.69\\ -8.85, -2.49\\ -7.16, -3.04\\ -7.16, -7.16, -7.16\\ -$	3.8% 0.4% 0.7% 8.1% 0.2% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4	3.0 3.1 2.8 2.9 2.9 2.9 3.0 3.0 3.0 3.1 2.9 2.9 3.0 3.0 2.7 2.9 2.9 2.9 2.9 2.9 2.9 2.9 2.9 2.9 2.9	
Chang CF 2015 150 29.30 22.50 128 11.80 26.90	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong SC 2011 Zhang MX 2018 Li JH 2008 Che YQ 2005 Liu XY 2016 Liu XY 2016 Liu XY 2016 Wang XH 2015 Sun HY 2005 Cao XM 2015 Zhang H 2009 Cao XM 2015 Zhang H 2009 Li SJ 2014 Tai SEGL 2011 Jia HB 2008 Zhang YC 2001 Zhang XX 2017 Zhang YC 2004 Zhang XX 2017 Zhang YC 2004 Zhang ZX 2010 Yu BQ 2003 Zhang HM 2004 Zhu L 2014 Yin HX 2004	40 40 41 41 43 44 46 47 51 52 55 56 60 60 60 60 60 62 66 65 56 66 67 4 73 95 50 50	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	40 41 43 44 47 51 55 56 58 60 60 61 62 58 862 75 70 70 70 390 100	25.30 17.31 17.56 16.20 10.20 13.55 16.20 14.67 23.30 16.40 19.60 19.60 19.50 17.88 15.45 15.40 13.40 15.40 17.80 14.55 4.21	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 1.42 7.92 5.91 10.80 8.10 9.37 7.50 7.90 5.80 1.42 7.92 5.91 10.80 8.10 8.10 9.37		$\begin{array}{c} -5.06\\ -5.71\\ -2.04\\ -0.30\\ -3.93\\ -7.80\\ -6.40\\ -2.31\\ -11.20\\ -3.70\\ -3.70\\ -3.70\\ -3.70\\ -8.22\\ -8.15\\ -5.67\\ -3.80\\ -5.61\\ -2.49\\ -5.10\\ -2.49\\ -0.01\end{array}$	$\begin{bmatrix} -5.79, -4.33\\ -8.31, -3.11\\ -2.84, -1.24\\ -2.85, 2.25\\ -9.03, -3.77\\ -5.76, 1.14\\ -1.358, -7.26\\ -9.03, -3.77\\ -5.76, 1.14\\ -1.358, -8.82\\ -1.558, -6.82\\ -1.558, -6.83\\ -1.858, -6.83\\ -1.58, -7.69\\ -6.83, -1.87\\ -7.04, -3.16\\ -7.69\\ -6.83, -1.87\\ -7.04, -3.16\\ -7.68, -3.44\\ -7.16, -3.04\\ -7.76, -3.04\\ -7.$	$\left \begin{array}{c}3.8\%\\0.4\%\\0.7\%\\8.1\%\\0.4\%\\0.2\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.7\%\\0.2\%\\0.6\%\\0.6\%\\0.5\%\\0.6\%\\0.5\%\\0.6\%\\0.7\%\\0.28\%\\0.7\%\\0.5\%\\0.6\%\\0.7\%\\0.5\%\\0.5\%\\0.5\%\\0.5\%\\0.5\%\\0.5\%\\0.5\%\\0.5$	3.0 3.1 2.8 2.6 2.9 2.9 2.9 3.0 3.0 3.0 3.0 3.1 2.9 3.0 2.7 2.9 2.9 3.1 3.1	
	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong XC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Che YQ 2005 Liu XY 2016 Wang XH 2015 Zhang H 2009 Zhang XD 2015 Zhang H 2009 Zhang XK 2017 Zhang YZ 2010 Yu BQ 2003 Zhang XX 2010 Zhang JP 2004 Zhu L 2014 Sun BJ 2014 Sun BJ 2013	40 40 41 41 43 44 46 46 47 51 52 55 56 60 60 60 60 62 66 5 5 66 65 5 66 74 73 95 100 120	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	40 41 43 44 44 47 51 55 56 66 60 61 62 58 862 75 70 73 30 900 100	25.30 17.31 17.56 16.20 13.55 16.20 14.67 23.30 16.40 16.50 19.50 19.50 19.50 17.88 15.45 27.10 13.40 15.40 13.40 14.57 13.40 14.54 14.51 16.30	1.98 6.87 1.88 6.50 4.54 2.00 8.10 9.37 7.50 7.90 5.80 3.60 1.42 7.90 5.81 10.80 8.10 7.40 8.10 7.40 8.203 7.70		-5.06 -5.71 -2.24 -0.30 -3.39 -7.80 -6.40 -2.31 -11.20 -3.70 -3.70 -3.70 -3.70 -8.20 -8.15 -5.10 -5.67 -3.80 -5.510 -5.40 -2.49 -0.01 -2.49 -0.01	$\begin{bmatrix} -5.79, -4.33\\ -8.31, -3.11\\ -2.84, -1.24\\ -1.284, -1.24\\ -1.284, -1.24\\ -1.285, -2.03\\ -8.35, -7.25\\ -9.03, -3.77\\ -5.76, -1.14\\ -6.14, -1.26\\ -1.25, -1.8, -8.82\\ -6.16, -1.24\\ -6.14, -1.26\\ -1.25, -1.8, -8.82\\ -8.6, -2.6\\ -9.6, -1.26\\ -9.58, -6.82\\ -8.6, -2.6\\ -9.6, -1.26\\ -9.58, -2.49\\ -6.11, -1.49\\ -7.16, -3.04\\ -2.78, -2.20\\ -5.41, -1.99\\ -5.$	$ \begin{array}{c} 3.8\% \\ 0.4\% \\ 0.7\% \\ 8.1\% \\ 0.4\% \\ 0.4\% \\ 0.4\% \\ 0.4\% \\ 0.4\% \\ 0.4\% \\ 1.3\% \\ 11.8\% \\ 0.4\% \\ 0.5\% \\ 0.5\% \\ 0.5\% \\ 0.5\% \\ 0.6\% \\ 28.5\% \\ 7.4\% \\ 0.8\% \\ 0.9\% \\$	3.0 3.1 2.8 2.6 2.9 2.9 3.0 3.0 3.0 3.0 2.7 2.9 2.9 3.1 3.1 3.1 3.1 3.0	
Common effect model 2036 1960 -3.17 [-3.33; -3.01] 100.0% Random effects model -4.31 [-5.75; -2.88]	Chen R 2015 Tian ZC 2008 Wang QY 2012 Xiong XC 2011 Zhang MX 2018 Shi JP 2008 Ma YX 2016 Li JH 2008 Che YQ 2005 Liu XY 2016 Che YQ 2005 Liu XY 2016 Wang XH 2015 Zhang H 2009 Zhang XD 2015 Zhang H 2009 Zhang XK 2017 Zhang YZ 2010 Yu BQ 2003 Zhang XX 2010 Zhang JP 2004 Zhu L 2014 Sun BJ 2014 Sun BJ 2013	40 40 41 41 43 44 46 47 51 55 56 60 60 60 60 60 60 60 60 60 60 60 60 60	$\begin{array}{c} 12.80 & 1.70 \\ 10.83 & 2.10 \\ 21.20 & 1.10 \\ 12.25 & 1.30 \\ 11.25 & 5.33 \\ 11.85 & 5.33 \\ 14.16 & 1.96 \\ 9.90 & 5.80 \\ 8.40 & 0.20 \\ 10.30 & 5.20 \\ 12.36 & 9.10 \\ 12.10 & 5.10 \\ 12.10 & 5.60 \\ 12.80 & 4.22 \\ 11.30 & 4.20 \\ 9.73 & 1.17 \\ 11.10 & 5.80 \\ 4.20 & 5.22 \\ 7.73 & 8.42 \\ 11.60 & 5.80 \\ 4.22 \\ 0.52 \\ 11.27 & 5.60 \\ 1.27 & 5.60 \\ 1.28 \\ 0.50 \\ 1.28 \\ 0.50 \\ 1.21 \\ 1.10 \\ $	40 41 43 44 44 47 51 55 56 60 60 61 62 58 86 20 60 61 62 75 70 73 90 0 100 116 121	25.30 17.31 17.56 16.20 10.20 13.55 16.20 14.67 23.30 16.40 19.60 10.60	1.98 6.87 1.88 6.54 2.00 8.10 9.37 7.50 7.80 7.90 5.80 3.60 3.60 3.60 3.60 3.60 3.60 3.80 7.92 5.91 10.80 7.40 0.98 2.03 7.750 7.50		$\begin{array}{c} -5.06\\ -5.71\\ -2.04\\ -0.30\\ -3.93\\ -7.80\\ -6.40\\ -2.31\\ -11.20\\ -3.70\\ -3.70\\ -3.70\\ -3.70\\ -8.20\\ -8.15\\ -5.10\\ -5.67\\ -3.80\\ -5.10\\ -2.49\\ -0.01\\ -3.70\\ -3.70\\ -5.50\end{array}$	$\begin{bmatrix} -5.79, -4.33\\ -8.31, -3.11\\ -2.84; -1.24\\ -2.85, -2.25\\ -9.03, -3.77\\ -5.76; 1.14\\ -1.26; -3.25\\ -9.03, -3.77\\ -5.76; 1.14\\ -1.26\\ -1.251, -8.89\\ -6.14; -1.24\\ -6.14; -1.26\\ -6.14; -1.24\\ -6.14; -7.69\\ -8.83; -1.87\\ -7.64; -3.16\\ -8.83; -1.27\\ -7.04; -3.16\\ -8.85; -2.49\\ -6.11; -1.49\\ -6.71; -7.69\\ -6.11; -1.49\\ -7.16; -3.04\\ -7.76; -2.27\\ -7.44; -3.16\\ -7.59; -0.57\\ -7.44; -3.16\\ -7.59; -0.57\\ -7.44; -3.367\\ -7.33; -3.67\\ -7.33; -3.67\\ -7.33; -3.67\\ -7.33; -3.67\\ -7.33; -3.67\\ -7.33; -3.67\\ -7.33; -3.67\\ -8.25\\ -8.25\\ -8.25\\ -9.25$	$\left \begin{array}{c}3.8\%\\0.4\%\\0.7\%\\8.1\%\\0.4\%\\0.2\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.4\%\\0.7\%\\0.2\%\\0.6\%\\0.6\%\\0.6\%\\0.6\%\\0.6\%\\0.6\%\\0.6\%\\0.6$	3.0 3.1 2.8 2.6 2.9 2.9 2.9 3.0 3.0 3.0 3.0 3.1 2.9 3.0 2.7 2.9 2.9 3.1 3.1	

FIGURE 5

Forest plot and meta-analysis of neurological function. (Note. CSS, Chinese Stroke Scale; CTs, conventional treatments; NIHSS, National Institutes of Health Stroke Scale; SXNI, shuxuening injection).

metabolism and nutrition of hypoxic brain cells via its antioxidant properties (Smith et al., 2002; Nash and Shah, 2015) and reduce the apoptosis of neuronal cells in brain tissue through the inhibition of multiple inflammatory responses and the modulation of oxidative stress levels (Dong et al., 2023). Moreover, SXNI can increase superoxide dismutase activity against oxidative damage caused by

Study		xperin Mean			Mean	ontrol SD	Mean Difference	MD	95%-CI	Weight (common)	
Huang JL 2010	60	81.50	16.80	60	69.30	15.10	- } -	12.20	[6.48; 17.92]	1.7%	11.6%
Li XL 2023	35	63.85	5.14	35	52.03	4.74		11.82	[9.50; 14.14]	10.3%	16.2%
Li YJ 2018	62	74.96	5.26	62	61.42	4.85		13.54	[11.76; 15.32]	17.4%	16.8%
Peng J 2021	37	22.15	2.46	37	15.57	2.61		6.58	[5.42; 7.74]	41.2%	17.3%
Wang DH 2023	60	66.37	12.31	60	60.56	10.38		5.81	[1.74; 9.88]	3.3%	13.9%
Xiao DF 2022	40	57.06	3.85	40	40.18	2.76	ê 	16.88	[15.41; 18.35]	25.5%	17.1%
Xie YQ 2004	30	70.37	19.55	30	54.21	18.32	÷ •	- 16.16	[6.57; 25.75]	0.6%	7.1%
Common effect model	324			324				11.08	[10.34; 11.83]	100.0%	
Random effects model								11.58	[8.27; 14.90]		100.0%
Heterogeneity: $I^2 = 96\%$, τ^2	² = 16.2	2359, p	< 0.01				-20 -10 0 10 20				
.SXNI plus CTs vs CT		s othe xperin				core ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(common)	(random)
Chang CF 2015	150	2.10	11.30	128	3.30	11.50		-1.20	[-3.89; 1.49]	13.4%	16.6%
Chen LY 2021	35	21.33	2.38	35	14.22	2.46		7.11	[5.98; 8.24]	75.6%	17.3%
Li SJ 2014	60	54.90	19.60	60	44.30	16.50		10.60	[4.12; 17.08]	2.3%	13.4%
Ma YX 2016	43	55.46	17.54	43	43.54	16.87		- 11.92	[4.65; 19.19]	1.8%	12.7%
Yu BQ 2003	66	62.10	18.20	75	68.00	17.70		-5.90	[-11.84; 0.04]	2.8%	14.0%
Zhang H 2009	60	54.80	19.50	58	44.20	16.30		10.60	[4.12; 17.08]	2.3%	13.4%
Zhao YX 2015	42	43.10	16.18	42	36.24	18.25	+	6.86	[-0.52; 14.24]	1.8%	12.6%
Common effect model	456			441			•	5.88	[4.90; 6.87]	100.0%	
Random effects model								5.43	[0.48; 10.39]		100.0%
Heterogeneity: $I^2 = 89\%$, τ^2	2 = 36.6	632, p	< 0.01						-		
							-15-10-5 0 5 10 15				

ischemia to protect muscle cells (Gao et al., 2007; Koyama et al., 2013; Powers and Lennon, 1999), and Ginkgolide B also can promote muscle regeneration by reviving osteocalcin–GPRC6A signalling (Wang et al., 2023). This may be the potential mechanism by which SXNI can reduce neurological deficits and improve limb function in AIS patients.

A centralized hospital monitoring study of the safety of SXNI injection in 9,735 patients showed that SXNI had a low incidence of AEs and good safety (Qu et al., 2023), which is consistent with our results. However, with the expanding application scope and increasing use frequency of SXNI in clinical practice, it is often abused. Reports of AEs related to SXNI were not uncommon. More than 80% of patients experienced AEs within 2 hours after administration (Chen, 2018; Gong and Shang, 2023), which prompted us to focus on monitoring the patient's condition during this time period. The occurrence of AEs to SXNI may be related to many factors, such as patient age, type of solvent, dosage, over-the-counter use, and coadministration (Wu, 2019). Therefore, we should pay attention to selecting the appropriate drug solvent, strictly follow the instructions for use, and try to avoid using other injections in combination.

In this review, 12.9% of the included studies were defined as moderate to high quality. Correct randomization and allocation concealment are important conditions for ensuring the minimization of selection bias; however, only 15 (12.9%) studies reported correct randomization methods, and none of the studies reported detailed allocation concealment, blinding, or implementation. Of all studies, 2.6% did not conduct intentionto-treat analysis and did not specify the reason for case dropout, 7.8% may not have completely reported outcomes, and none was registered in advance. Although all outcomes except CER showed significant heterogeneity, our subgroup analysis and mixed-effect regression analysis did not reveal the source of heterogeneity. Sensitivity analysis revealed differences in BI scores between SXNI plus CTs and CTs plus other injections when five studies (Chen, 2021; Li, 2014; Ma, 2016; Zhang et al., 2009; Zhao, 2015) were excluded one by one. The different manufacturers of SXNI, large sample size spans, different age-inclusion criteria, and populations in the different regions of these five studies may be potential sources of heterogeneity. The overall level of evidence for each outcome ranged from very low to low quality. The reasons for this were mainly the low methodological quality of the included studies, high heterogeneity among the included studies, and potential publication bias. Consequently, future RCTs with large sample sizes from multiple centers should be rigorously conducted in accordance with the consolidated standards of reporting trials (CONSORT) and should be registered in advance on the registration platform (Schulz et al., 2010).

4.2 Compared with previous studies

Our results suggested that SXNI in the treatment of AIS could not only increase CER and improve neurological function and ADL but also had good safety, which was consistent with the results of five systematic reviews previously published in 2011, 2012, and 2016 (Yan, et al., 2011; Xi et al., 2012; Zheng et al., 2012; Cai and Jiang, 2012; Tan, et al., 2016). We included patients who had AIS within

TABLE 3 Summary of findings according to the Grading Recommendations Assessment, Development, and Evaluations (GRADE) tool. (Note. CI, confidence interval; CTs, conventional treatments; MD, mean
difference; RR, risk ratio; SXNI, shuxuening injection).

interence, kk	t, fisk ratio, ski	NI, snuxuer	ning injection).									
			Certainty a	ssessment			No of	patients	E	ffect	Certainty	Importanc
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SXNI plus CTs	CTs alone	Relative (95% CI)	Absolute (95% CI)		
A. SXNI plus	CTs versus CT	s alone		<u>.</u>								
Clinical Effec	ctive Rate											
32	randomised trials	seriousa	not serious	not serious	not serious	publication bias strongly suspectedd	1397/ 1550 (90.1%)	1119/ 1506 (74.3%)	RR 1.21 (1.17 to 1.25)	156 more per 1,000(from 126 more to 186 more)	⊕⊕000 Low	CRITICAL
Chinese Stro	oke Scale											
10	randomised trials	very seriousb	very seriousc	not serious	not serious	none	581	536	-	MD 5.01 lower (7.38 lower to 2.65 lower)	⊕000 Very low	IMPORTANT
National Inst	titute of Health	Stroke Sc	ale									
11	randomised trials	not serious	very seriousc	not serious	not serious	publication bias strongly suspectedd	563	563	-	MD 4 lower (5.22 lower to 2.78 lower)	⊕000 Very low	IMPORTAN
Barthel Inde	x	I					1		1			
7	randomised trials	not serious	very seriousc	not serious	not serious	none	324	324	-	MD 11.58 higher (8.27 higher to 14.9 higher)	⊕⊕OO Low	IMPORTANT
B. SXNI plus	CTs versus CT	s plus othe	er injections	1			1		1	1		
Clinical Effici	iency Rate											
70	randomised trials	very seriousb	not serious	not serious	not serious	publication bias strongly suspectedd	3528/ 3910 (90.2%)	2849/ 3763 (75.7%)	RR 1.18 (1.15 to 1.21)	136 more per 1,000 (from 114 more to 159 more)		CRITICAL
Chinese Stro	oke Scale											
34	randomised trials	very seriousb	very seriousc	not serious	not serious	none	2036	1960	-	MD 4.31 lower (5.75 lower to 2.88 lower)	⊕000 Very low	IMPORTAN
National Inst	titutes of Healt	h Stroke S	cale									·
5	randomised trials	very seriousb	very seriousc	not serious	not serious	none	217	217	-	MD 2.28 lower (3.41 lower to 1.16 lower)	⊕000 Very low	IMPORTAN

			Certainty assessment	ssessment			No of p	No of patients	Ш	Effect	Certainty	Certainty Importance
No of studies	Study design	Risk of bias	Inconsistency Indirectness	Indirectness	Imprecision	Other considerations	SXNI plus CTs	CTs alone	Relative (95% CI)	Absolute (95% Cl)		
Barthel Index	×											
м	randomised trials	very seriousb	very seriousc	not serious	not serious	publication bias strongly suspectedd	456	441	ı	MD 5.43 higher (0.48 higher to 10.39 higher)	#000 Very low	IMPORTANT
Note: CI, confide Evalanations:	nce interval; CTs,	conventional	Note: CI, confidence interval; CTs, conventional treatments, MD, mean difference; RR, risk ratio, SXNI, shuxuening injection.	ference; RR, risk ratio;	SXNI, shuxuening inje	ction.		_		_	_	

14 days; however, Xi et al. and Zheng et al. included patients whose stroke occurred within 72 h and 7 days, respectively. According to the use requirements of SXNI, we included only adult stroke patients, but previous studies did not limit the age of AIS patients, which may have affected the scope of its application. Compared with previous meta-analyses (Yan, et al., 2011; Xi et al., 2012; Zheng et al., 2012; Cai and Jiang, 2012; Tan, et al., 2016), our study used more comprehensive outcomes (including CER, neurological function, ADL, and AEs) to evaluate the efficacy and safety of SXNI as an add-on therapy for AIS. However, Yan et al. included only 14 RCTs and did not report neurological deficit scores for outcome measures. Cai et al. only observed the CER of SXNI in AIS patients based on 22 RCTs. Tan et al. did not evaluate the effect of SXNI on the ability of patients with AIS to perform ADL. Moreover, the studies included in the previous meta-analyses (Yan, et al., 2011; Xi et al., 2012; Zheng et al., 2012; Cai and Jiang, 2012; Tan, et al., 2016) were all published before 2016, and many RCTs focusing on SXNI for AIS have been reported since 2016; therefore, our literature search deadline was 2023 to update the evidence.

4.3 Implications for practice and research

Our findings supported the clinical use of SXNI as an add-on treatment for AIS patients with a low level of evidence. Moreover, because no long-term follow-up studies have been performed to assess the effect of SXNI on the long-term prognosis of AIS patients, our study can only confirm that an intervention duration of 14–30 days with SXNI can effectively improve the neurological function and ADL of AIS patients. The usual daily dose of SXNI was 20 mL, and the most frequent treatment duration was 14 days. The five most common symptoms related to AEs were dizziness, flushing, palpitations, nausea, and headache, which is consistent with previous studies (Qu et al., 2023; Gong and Shang, 2023). Cardiovascular system events were the most common AEs of SXNI for AIS patients. Therefore, in clinical practice, SXNI should be used in strict accordance with the instructions, and patients should be monitored within 2 h after SXNI administration.

In this review, most (87.1%) included studies were judged as low quality. The lack of a detailed description of allocation concealment and blinding methods is a common problem in most studies. In all, 7.8% of the studies may have had a selective reporting bias. The included studies were all single-center RCTs conducted in China, which may mask the efficacy of SXNI in stroke patients of different ethnicities. Most of the studies were conducted in cities, and there is a lack of studies on SXNI for AIS in rural or primary medical institutions, while AIS patients in rural and primary medical institutions are in urgent need of effective and convenient drugs or technologies. SXNI has the advantages of being easy to use and safe. If SXNI is indeed effective in improving the prognosis of AIS patients, it will compensate for the deficiency caused by limited access to IVT and/or EVT. Large-sample, multicenter, placebocontrolled RCTs, especially in rural or primary medical institutions, should be conducted in the future. Moreover, all RCTs should be registered in an internationally recognized clinical trial registration platform and reported in accordance with the CONSORT guidelines.

More than 75% of the studies were those with a higher risk of overall bias

the studies was substantial.

There was a risk of publication bias

. Heterogeneity among

4.4 Limitations and advantages

Some limitations of this study should be noted. First, all included trials were conducted in China and published in Chinese, which may have led to selection bias and publication bias and reduced the generalizability of the results to the applicable population. Second, most of the included studies were of low quality and had significant heterogeneity, which led to a low level of evidence.

There are also some advantages in our study. First, we carried out an extensive literature search, including seven databases and two clinical trial registration platforms, to obtain as many relevant studies as possible. Second, two reviewers independently performed literature screening, data extraction, and quality evaluation and cross-checked to ensure the accuracy of the data. Third, we conducted a sensitivity analysis, subgroup analysis, and mixed-effects meta-regression analysis to test the robustness of the meta-analysis results. We also assessed the level of evidence for each outcome based on the GRADE tool.

5 Conclusion

SXNI, as an add-on therapy, maybe safe and significantly improved the clinical efficacy, neurological function, and ADL of patients with AIS. However, due to the low quality of the included studies and the very low to low level of evidence in the meta-analysis results, more standardized, large sample, multicenter, and long follow-up RCTs are needed to confirm the efficacy and safety of SXNI for AIS.

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.

Author contributions

JZ: Writing-review and editing, Writing-original draft, Methodology, Funding acquisition, Data curation, Conceptualization. XX: draft, Writing-original Project administration. YZ: draft, Writing-original Project administration. LL: Writing-original draft, Data curation, Project administration. HC: Writing-review and editing, Funding acquisition. LZ: Writing-review and editing, Conceptualization.

References

Ahlemeyer, B., and Krieglstein, J. (2003). Neuroprotective effects of Ginkgo biloba extract. Cell Mol. Life Sci. 60 (9), 1779–1792. doi:10.1007/s00018-003-3080-1

Bhatia, R., Hill, M. D., Shobha, N., Menon, B., Bal, S., Kochar, P., et al. (2010). Low rates of acute recanalization with intravenous recombinant tissue plasminogen activator in ischemic stroke: real-world experience and a call for action. *Stroke* 41 (10), 2254–2258. doi:10.1161/STROKEAHA.110.592535

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This study was funded by Medical Scientific Research Foundation of Guangdong Province (No. A2022239), special project of Science and Technology of Traditional Chinese Medicine of Guangdong Provincial Hospital of Chinese Medicine (No. YN2020QN23), Guangdong Basic and Applied Basic Research Foundation (No. 2022A1515220025), and special project of Lingnan modernization of traditional Chinese medicine in 2019 Guangdong Provincial R & D Program (No. 2020B111100008). This study was also funded by the project of Traditional Chinese medicine rehabilitation talent training program of the Traditional Chinese Medicine Bureau of Guangdong Province (No. 01020184). The funders had no influence on the study design, data collection and analysis, decision to publish, or manuscript preparation.

Acknowledgments

We would like to thank all graduate students in the Department of Rehabilitation from Guangdong Provincial Hospital of Chinese Medicine for their assistance in finishing this paper. We also thank Home for Researchers editorial team (www.home-for-researchers. com) for English language editing.

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphar.2024.1407669/ full#supplementary-material

Brott, T., Adams, H. P., Jr, Olinger, C. P., Marler, J. R., Barsan, W. G., Biller, J., et al. (1989). Measurements of acute cerebral infarction: a clinical examination scale. *Stroke* 20 (7), 864–870. doi:10.1161/01.str.20.7.864

Cai, L. M., and Jiang, J. Z. (2012). Summary analysis of the efficacy of Shuxuening injection for acute cerebral infarction. *Hebei Med. J.* 34 (8), 1217–1219. doi:10.3969/j. issn.1002-7386.2012.08.058

Chandrasekaran, K., Mehrabian, Z., Spinnewyn, B., Drieu, K., and Fiskum, G. (2001). Neuroprotective effects of bilobalide, a component of the Ginkgo biloba extract (EGb 761), in gerbil global brain ischemia. *Brain Res.* 922 (2), 282–292. doi:10.1016/s0006-8993(01)03188-2

Chen, J. (2018). Clinical analysis of adverse reactions of Shuxuening injection. J. Med. Theory Pract. 31 (3), 425–426. doi:10.19381/j.issn.1001-7585.2018.03.065

Chen, L. Y. (2021). Clinical effect of Shuxuening injection in the adjuvant treatment of acute cerebral infarction. *Chin. J. Clin. Ration. Drug Use* 14 (22), 47–49. doi:10.15887/j. cnki.13-1389/r.2021.22.017

Chinese Society of Neurology, Chinese Stroke Society (2018). Chinese guidelines for diagnosis and treatment of acute ischemic stroke. *Chin. J. Neurol.* 51, 666–682. doi:10. 3760/cma.j.issn.1006-7876.2018.09.004

Cui, Q., Zhang, Y. L., Ma, Y. H., Yu, H. Y., Zhao, X. Z., Zhang, L. H., et al. (2020). A network pharmacology approach to investigate the mechanism of Shuxuening injection in the treatment of ischemic stroke. *J. Ethnopharmacol.* 257, 112891. doi:10.1016/j.jep. 2020.112891

Diamond, B. J., Shiflett, S. C., Feiwel, N., Matheis, R. J., Noskin, O., Richards, J. A., et al. (2000). Ginkgo biloba extract: mechanisms and clinical indications. *Archives Phys. Med. rehabilitation* 81 (5), 668–678. doi:10.1016/s0003-9993(00)90052-2

Ding, Y. B. (2018). Effect of Shuxuening injection combined with Xingnao Kaiqiao acupuncture on blood lipid and neurological function in patients with cerebral infarction. *Clin. Res. Pract.* 3 (18), 119–120. doi:10.19347/j.cnki.2096-1413.201818055

Dong, W., Gong, T., Zhao, S., Wen, S., Chen, Q., Jiang, M., et al. (2023). A novel extract from Ginkgo biloba inhibits neuroinflammation and maintains white matter integrity in experimental stroke. *Neuroscience* 523, 7–19. doi:10.1016/j.neuroscience. 2023.05.015

Fourth Session of Chinese National Cerebrovascular Conference (1996). Scoring criteria for clinical neurological deficit in stroke patients (1995). *Chin. J. Neurol.* 29 (6), 381–383.

Gao, J., Zhou, N., Hu, J. J., and Zhang, H. X. (2007). Protection of shuxuening injection on focal cerebral ischemic in rat. *Chin. J. Rehabilitation Theory Pract.* (08), 712–713. doi:10.3969/j.issn.1006-9771.2007.08.005

GBD 2019 Stroke Collaborators (2021). Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol.* 20 (10), 795–820. doi:10.1016/S1474-4422(21)00252-0

Gong, T., and Shang, B. (2023). Rationality and safety evaluation of the use of Shuxuening injection. J. Navy Med. 44 (5), 524–526. doi:10.3969/j.issn.1009-0754.2023. 05.023

Guidetti, C., Paracchini, S., Lucchini, S., Cambieri, M., and Marzatico, F. (2001). Prevention of neuronal cell damage induced by oxidative stress *in-vitro*: effect of different Ginkgo biloba extracts. *J. Pharm. Pharmacol.* 53 (3), 387–392. doi:10.1211/ 0022357011775442

Gumbinger, C., Gruschka, P., Böttinger, M., Heerlein, K., Barrows, R., Hacke, W., et al. (2012). Improved prediction of poor outcome after thrombolysis using conservative definitions of symptomatic hemorrhage. *Stroke* 43 (1), 240–242. doi:10. 1161/STROKEAHA.111.623033

Hasan, T. F., Hasan, H., and Kelley, R. E. (2021). Overview of acute ischemic stroke evaluation and management. *Biomedicines* 9 (10), 1486. doi:10.3390/biomedicines9101486

Higgins, J. P. T., and Green, S. (2011). Cochrane handbook for systematic reviews of interventions. London: The Cochrane Collaboration.

Jiang, J. C., Jiang, Y. L., and Wen, J. (2023). Cognitive load theory perspectives on Ma wanli's fundamentals of traditional Chinese medicine the inspiration of English translation and interpretation of the core concept of qi. J. Guangxi Univ. Chin. Med. 26 (02), 86–91. doi:10.3969/j.issn.2095-4441.2023.02.022

Jørgensen, H. S., Nakayama, H., Raaschou, H. O., and Olsen, T. S. (1999). Stroke. Neurologic and functional recovery the Copenhagen stroke study. *Phys. Med. rehabilitation Clin. N. Am.* 10 (4), 887–906. doi:10.1016/s1047-9651(18)30169-4

Koyama, H., Nojiri, H., Kawakami, S., Sunagawa, T., Shirasawa, T., and Shimizu, T. (2013). Antioxidants improve the phenotypes of dilated cardiomyopathy and muscle fatigue in mitochondrial superoxide dismutase-deficient mice. *Molecules* 18 (2), 1383–1393. doi:10.3390/molecules18021383

Kwah, L. K., and Diong, J. (2014). National Institutes of Health stroke scale (NIHSS). J. Physiother. 60 (1), 61. doi:10.1016/j.jphys.2013.12.012

Li, L. D., Zhou, Y., and Shi, S. F. (2023). Edaravone combined with Shuxuening versus edaravone alone in the treatment of acute cerebral infarction: a systematic review and meta-analysis. *Medicine* 102 (9), e32929. doi:10.1097/MD.00000000032929

Li, S., Zhang, X., Fang, Q., Zhou, J., Zhang, M., Wang, H., et al. (2017). Ginkgo biloba extract improved cognitive and neurological functions of acute ischaemic stroke: a randomised controlled trial. *Stroke Vasc. neurology* 2 (4), 189–197. doi:10.1136/svn-2017-000104

Li, S. J. (2014). Clinical effect of Shuxuening injection in the treatment of acute cerebral infarction. *Jilin Med. J.* 35 (12), 2560. doi:10.3969/j.issn.1004-0412.2014.12.050

Ma, Y. X. (2016). Clinical effect and safety analysis of Shuxuening in the treatment of cerebral infarction. *China Health Care & Nutr.* 26 (29), 49. doi:10.3969/j.issn.1004-7484.2016.29.057

Mahoney, F. I., and Barthel, D. W. (1965). Functional evaluation: the barthel index. *Md. state Med. J.* 14, 61–65.

Nash, K. M., and Shah, Z. A. (2015). Current perspectives on the beneficial role of Ginkgo biloba in neurological and cerebrovascular disorders. *Integr. Med. insights* 10, 1–9. doi:10.4137/IMI.S25054

National Administration of Traditional Chinese Medicine (1994). Standard for diagnosis and efficacy of Chinese medicine syndrome. Nanjing: Nanjing University Press.

Oskouei, D. S., Rikhtegar, R., Hashemilar, M., Sadeghi-Bazargani, H., Sharifi-Bonab, M., Sadeghi-Hokmabadi, E., et al. (2013). The effect of Ginkgo biloba on functional outcome of patients with acute ischemic stroke: a double-blind, placebo-controlled, randomized clinical trial. *J. Stroke Cerebrovasc. Dis.* 22 (8), e557–e563. doi:10.1016/j. jstrokecerebrovasdis.2013.06.010

Ovbiagele, B., Goldstein, L. B., Higashida, R. T., Howard, V. J., Johnston, S. C., Khavjou, O. A., et al., and American Heart Association Advocacy Coordinating Committee and Stroke Council (2013). Forecasting the future of stroke in the United States: a policy statement from the American heart association and American stroke association. *Stroke* 44 (8), 2361–2375. doi:10.1161/STR. 0b013e31829734f2

Oyama, Y., Chikahisa, L., Ueha, T., Kanemaru, K., and Noda, K. (1996). Ginkgo biloba extract protects brain neurons against oxidative stress induced by hydrogen peroxide. *Brain Res.* 712 (2), 349–352. doi:10.1016/0006-8993(95)01440-3

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372, n71. doi:10.1136/bmj.n71

Powers, S. K., and Lennon, S. L. (1999). Analysis of cellular responses to free radicals: focus on exercise and skeletal muscle. *Proc. Nutr. Soc.* 58 (4), 1025–1033. doi:10.1017/s0029665199001342

Qu, Y., Ma, X. J., Li, Q. H., Li, H. L., Zhao, X. C., Sun, X. H., et al. (2023). Intensive hospital monitoring study on safety of 9735 cases of Shuxuening Injection. *Chin. Traditional Herb. Drugs* 54 (10), 3253–3260. doi:10.7501/j.issn.0253-2670.2023. 10.022

Rochmah, T. N., Rahmawati, I. T., Dahlui, M., Budiarto, W., and Bilqis, N. (2021). Economic burden of stroke disease: a systematic review. *Int. J. Environ. Res. Public Health* 18 (14), 7552. doi:10.3390/ijerph18147552

Rosa, J. L., Alves, M., Ferreira, P., Papoila, A. L., and Nunes, A. P. (2022). Previous disability and benefit of acute phase therapy in functional prognosis of selected patients with ischemic stroke. *J. Stroke Cerebrovasc. Dis.* 31 (1), 106183. doi:10.1016/j. jstrokecerebrovasdis.2021.106183

Schulz, K. F., Altman, D. G., Moher, D., and CONSORT Group (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann. Intern Med.* 152 (11), 726–732. doi:10.7326/0003-4819-152-11-201006010-00232

Shi, C., Zhao, L., Zhu, B., Li, Q., Yew, D. T., Yao, Z., et al. (2009). Protective effects of Ginkgo biloba extract (EGb761) and its constituents quercetin and ginkgolide B against beta-amyloid peptide-induced toxicity in SH-SY5Y cells. *Chem. Biol. Interact.* 181 (1), 115–123. doi:10.1016/j.cbi.2009.05.010

Singh, S. K., Srivastav, S., Castellani, R. J., Plascencia-Villa, G., and Perry, G. (2019). Neuroprotective and antioxidant effect of Ginkgo biloba extract against AD and other neurological disorders. *Neurotherapeutics* 16 (3), 666–674. doi:10.1007/s13311-019-00767-8

Smith, J. V., Burdick, A. J., Golik, P., Khan, I., Wallace, D., and Luo, Y. (2002). Antiapoptotic properties of Ginkgo biloba extract EGb 761 in differentiated PC12 cells. *Cell Mol. Biol*(*Noisy-le-grand*) 48 (6), 699–707.

Smith, P. F., Maclennan, K., and Darlington, C. L. (1996). The neuroprotective properties of the Ginkgo biloba leaf: a review of the possible relationship to platelet-activating factor (PAF). *J. Ethnopharmacol.* 50 (3), 131–139. doi:10.1016/0378-8741(96) 01379-7

Tan, D., Wu, J. R., Liu, S., and Zhang, B. (2016). Meta-analysis of efficacy of shuxuening injection in the treatment of cerebral infarction. *Chin. J. Pharmacoepidemiol.* 25 (8), 492–498.

Tian, J., Chen, L., Huang, X. L., Ding, Y. R., Wang, W., Huang, X. Y., et al. (2024). Understanding and relationship of qi and xue in traditional Chinese and western medicine. *Chin. J. Med. Guide* 26 (02), 171–175. doi:10.3969/j.issn.1009-0959.2024. 02.020

Wang, B. Y., Chen, Y. F., Hsiao, A. W., Chen, W. J., Lee, C. W., and Lee, O. K. (2023). Ginkgolide B facilitates muscle regeneration via rejuvenating osteocalcin-mediated bone-to-muscle modulation in aged mice. *J. Cachexia Sarcopenia Muscle* 14 (3), 1349–1364. doi:10.1002/jcsm.13228

Wassélius, J., Arnberg, F., von Euler, M., Wester, P., and Ullberg, T. (2022). Endovascular thrombectomy for acute ischemic stroke. *J. Intern. Med.* 291 (3), 303–316. doi:10.1111/joim.13425

Wu, T. T. (2019). Retrospective analysis of adverse drug reaction of shuxuening injection in xi'an from 2013 to 2017. *Her. Med.* 38 (1), 49–53. doi:10.3870/j.issn.1004-0781.2019.01.011

Xi, B. C., Zhang, C., and Sun, L. L. (2012). Meta analysis of Shuxuening injection in treatment of patients with acute cerebral infarction. *Pharm. Care Res.* 12 (5), 354–357. doi:10.5428/pcar20120512

Yan, J., Wang, X. W., Zhou, J., Jing, J., Wang, C. X., and Li, J. J. (2011). Meta-analysis of shuxuening injection in the treatment for cerebral infarction. *Chin. J. Rehabil. Theory Pract.* 17 (9), 884–886. doi:10.3969/j.issn.1006-9771.2011.09.025

Zhang, A. L., Zhang, J. W., Sun, J. N., and Xu, Q. P. (2005). Progress on the mechanism of anti-ischemic action of Ginkgo biloba extracts. *China Pharm.* 16 (08), 626–629. doi:10.3969/j.issn.1001-0408.2005.08.031

Zhang, H., Zhou, M., and Zhang, J. J. (2009). The therapeutic effect of Shuxuening injection on acute cerebral infarction and its mechanism. *China J. Traditional Chin. Med. Pharm.* 24 (01), 81–84. doi:10.3969/j.issn.1004-7484(s).2013.09.542

Zhang, Z. W. (2019). Clinical observation of Pingganditantongluotang combined with Shuxuening injection in the treatment of cerebral infarction in the convalescent phase. *Guangming J. Chin. Med.* 34 (21), 3336–3338. doi:10.3969/j.issn.1003-8914.2019.21.047

Zhao, Y. X. (2015). Clinical observation of Shuxuening in the treatment of cerebral infarction. J. Front. Med. 5 (36), 87–88. doi:10.3969/j.issn.2095-1752.2015.36.086

Zheng, W. K., Zhang, L., and Shang, H. C. (2012). Systematic review on shuxuening injection in treating acute cerebral infarction. *China Licens. Pharm.* 9 (12), 33-41. doi:10.3969/j.issn.1672-5433.2012.12.007

Zheng, X. Y. (2002). *Guiding principles for clinical study of new Chinese medicines*. Beijing: China Medical Science Press.