Postprint: Meta-Analysis of the Prevalence and Influencing Factors of Cognitive Impairment in Elderly Stroke Patients in China

Authors: Jian Qiufeng, Xu Ronghua, Yao Qian, Zhou Yuanyuan, Yao Qian

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Abstract

Background China has entered a fully aging society. Stroke is the leading cause of death and disability among adults in China, and post-stroke cognitive impairment has become an important cause of long-term disability and decreased quality of life in stroke patients. Objective To determine the prevalence and influencing factors of cognitive impairment in elderly stroke patients through Meta-analysis. Methods Computer searches were conducted on CNKI, Wanfang Data Knowledge Service Platform, VIP, Chinese Biomedical Literature Database (CBM), PubMed, Embase, Cochrane Library, and Web of Science to collect cohort, case-control, and cross-sectional studies on influencing factors of cognitive impairment in elderly stroke patients published from database inception to February 12, 2023. Two researchers independently screened the literature and extracted data, after which the quality of included studies was assessed. Meta-analysis of the prevalence and influencing factors of cognitive impairment in elderly stroke patients in China was performed using Stata 14.0 software. Results A total of 46 articles were included, involving 3,281 cases of cognitive impairment patients and 27 influencing factors. Meta-analysis results showed that the prevalence of cognitive impairment in elderly stroke patients in China was 42.4% 〔95%CI (36.6%, 48.3%〕. Female gender (OR=4.167, 〔95%CI (1.937,8.967,P<0.001〕, hypertension (OR=2.824,〔95%CI(2.292,3.481,P<0.001〕, systolic blood pressure (OR=1.572,〔95%CI(1.444,1.711,P<0.001〕, diabetes mellitus 〔OR=3.344, 95%CI (2.611, 4.284), P<0.001〕, hyperlipidemia 〔OR=2.228, 95%CI (1.091, 4.547), P=0.028〕, carotid plaque 〔OR=2.544, 95%CI (1.076, 6.014), P=0.033〕, infarct location (frontal lobe, temporal lobe) 〔frontal lobe: OR=1.615, 95%CI (1.167, 2.235), P=0.004; temporal lobe: OR=1.739, 95%CI (1.246, 2.427), P=0.001〕, multiple cerebral infarctions〔OR=2.583, 95%CI (2.009, 3.321), P<0.001〕, cerebral atrophy〔OR=2.943, 95%CI (1.938, 4.469), P<0.001〕, homocysteine (Hcy)〔OR=2.209, 95%CI (1.656, 2.948), P<0.001〕, hyperhomocysteinemia〔OR=3.043, 95%CI (2.092, 4.426), P<0.001〕, high-sensitivity C-reactive protein (hs-CRP) 〔OR=4.331，95%CI (1.756，10.685)，P=0.001〕, and National Institutes of Health Stroke Scale (NIHSS) >10 points〔OR=1.977，95%CI (1.320，2.961)，P=0.001〕 were identified as 13 risk factors for cognitive impairment in elderly stroke patients in China. Conclusion The prevalence of cognitive impairment in elderly stroke patients in China is relatively high (42.4%), and female gender, hypertension, systolic blood pressure, diabetes mellitus, hyperlipidemia, carotid plaque, infarct location (frontal lobe, temporal lobe), multiple cerebral infarctions, cerebral atrophy, Hcy, hyperhomocysteinemia, hs-CRP, and NIHSS are risk factors for cognitive impairment in elderly stroke patients in China.

Full Text

Preamble

A Meta-analysis of the Prevalence and Influencing Factors of Post-stroke Cognitive Impairment in Chinese Elderly Patients

JIAN Qiufeng[1], XU Ronghua[2], YAO Qian[3], *ZHOU Yuanyuan*[1]

[1]*School of Nursing, Chengdu University of Traditional Chinese Medicine, Chengdu 610075, China*

[2]*Department of Neurosurgery, Chengdu Second People's Hospital, Chengdu 610017, China*

[3]*Department of Nursing, Chengdu Second People's Hospital, Chengdu 610017, China*

Corresponding author: YAO Qian, Professor of Nursing; E-mail: qianyaocdsdermyy@163.com

Abstract

Background: China has entered a comprehensive aging society, and stroke is the leading cause of death and disability among adults in China. Post-stroke cognitive impairment has become an important cause of long-term disability and quality of life decline in stroke patients. **Objective:** To clarify the prevalence and influencing factors of cognitive impairment in elderly stroke patients through meta-analysis. **Methods:** CNKI, Wanfang Data Knowledge Service Platform, VIP, China Biology Medicine disc (CBM), PubMed, Embase, Cochrane Library, and Web of Science were systematically searched to collect cohort, case-control, and cross-sectional studies on influencing factors of cognitive impairment in elderly stroke patients from inception to February 12, 2023. Two researchers independently screened literature and extracted data. Literature quality assessment was performed, and meta-analysis of prevalence and influencing factors of cognitive impairment in Chinese elderly stroke patients was conducted using Stata 14.0 software. **Results:** A total of 46 studies were included, involving 3,281 cases of cognitive impairment and 27 influencing factors. Meta-analysis results showed that the prevalence of cognitive impairment in Chinese elderly stroke patients was 42.4% [95%CI (36.6%, 48.3%)]. Thirteen factors were identified as risk factors for cognitive impairment: female gender (OR=4.167, 95%CI (1.937, 8.967), P<0.001), hypertension (OR=2.824, 95%CI (2.292, 3.481), P<0.001), systolic blood pressure (OR=1.572, 95%CI (1.444, 1.711), P<0.001), diabetes mellitus (OR=3.344, 95%CI (2.611, 4.284), P<0.001), hyperlipidemia (OR=2.228, 95%CI (1.091, 4.547), P=0.028), carotid plaque (OR=2.544, 95%CI (1.076, 6.014), P=0.033), infarction location (frontal lobe, temporal lobe) (frontal lobe: OR=1.615, 95%CI (1.167, 2.235), P=0.004; temporal lobe: OR=1.739, 95%CI (1.246, 2.427), P=0.001), multiple cerebral infarction (OR=2.583, 95%CI (2.009, 3.321), P<0.001), encephalanalosis (OR=2.943, 95%CI (1.938, 4.469), P<0.001), homocysteine (Hcy) (OR=2.209, 95%CI (1.656, 2.948), P<0.001), hyperhomocysteinemia (OR=3.043, 95%CI (2.092, 4.426), P<0.001), high-sensitivity C-reactive protein (hs-CRP) (OR=4.331, 95%CI (1.756, 10.685), P=0.001), and NIHSS score >10 (OR=1.977, 95%CI (1.320, 2.961), P=0.001). **Conclusion:** The prevalence of cognitive impairment in Chinese elderly stroke patients is high (42.4%). Female gender, hypertension, systolic blood pressure, diabetes mellitus, hyperlipidemia, carotid plaque, infarction location (frontal and temporal lobes), multiple cerebral infarction, encephalanalosis, Hcy, hyperhomocysteinemia, hs-CRP, and NIHSS score >10 are risk factors for cognitive impairment in Chinese elderly stroke patients.

[**Key words**] Cognition disorders; Post-stroke cognitive impairment; Aged; Prevalence rate; Influencing factors; Meta-analysis; China

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Introduction

According to the 2020 seventh national population census bulletin, the population aged 60 and above accounted for 18.70% (264 million) of China's total population, and those aged 65 and above accounted for 13.50% (190 million) [1]. All provinces, municipalities, and autonomous regions except Tibet have entered an aging society, with 12 regions exceeding the super-aging standard of 14% elderly population aged 65 and above [1]. China has thus entered a comprehensive aging society.

Stroke is brain injury caused by blocked blood perfusion, with approximately 70% of strokes resulting from occlusion of major cerebral arteries [2] or sudden rupture of cerebral blood vessels. It can be classified into ischemic stroke (cerebral infarction) and hemorrhagic stroke [3]. Global Burden of Disease Study (GBD) data show that stroke is the leading cause of death and disability among adults in China, characterized by high incidence, high disability rate, high mortality, high recurrence rate, and high economic burden [4]. The 2019 stroke high-risk population screening and intervention project covering 451 screening sites across 31 provinces revealed that 50.81% of stroke patients in China were over 60 years old, with the 60-69 age group accounting for the highest proportion at 28.69% [4].

Post-stroke cognitive impairment specifically refers to cognitive decline occurring within 6 months after stroke, defined as "a series of syndromes that meet the diagnostic criteria for cognitive impairment after the clinical event of stroke, emphasizing the potential causal relationship between stroke and cognitive impairment and the relevance of clinical management between the two" [5]. Cognitive impairment is an important cause of long-term disability and quality of life decline in stroke patients, with approximately half of patients developing cognitive impairment within the first year after stroke [6]. Therefore, this study aims to explore the prevalence and influencing factors of cognitive impairment in Chinese elderly stroke patients through meta-analysis, providing reference for effective clinical intervention and prevention.

Methods

1.1 Search Strategy

We systematically searched CNKI, Wanfang Data Knowledge Service Platform, VIP, China Biology Medicine disc (CBM), PubMed, Embase, Cochrane Library, and Web of Science databases from inception to February 12, 2023. The search combined subject headings with free-text terms. Chinese search terms included stroke, intracranial embolism and thrombosis, intracranial hemorrhage, cognitive dysfunction, risk factors, and influencing factors. English search terms included stroke*, Cerebrovascular Accident*, Cognitive Dysfunction*, Cognitive defect*, Risk Factor*, and Influencing Factor*. Specific search strategies are shown in Table 1 .

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Study types: cohort, case-control, and cross-sectional studies; (2) Study subjects: Chinese population aged $ $60 years meeting stroke diagnostic criteria; (3) Outcome indicator: occurrence of cognitive impairment; (4) Chinese or English language publications.

Exclusion criteria: (1) Study subjects with diseases other than stroke affecting cognitive impairment (e.g., epilepsy, leukoaraiosis); (2) Review articles; (3) Studies unable to provide valid data; (4) Studies with unavailable full text.

1.3 Literature Screening and Quality Assessment

Two researchers independently screened literature using a three-step method: initial screening of titles and abstracts, full-text review for data extraction, and consensus through discussion when disagreements arose. Data were compiled using Excel, including author, year, study location, and other information. The Newcastle-Ottawa Scale (NOS) [7] was used to assess quality of cohort and case-control studies (1-3 points = low quality, 4-6 points = moderate quality, 7-9 points = high quality). The Agency for Healthcare Research and Quality

(AHRQ) criteria [8] were used for cross-sectional studies (0-3 points = low quality, 4-7 points = moderate quality, 8-11 points = high quality). Final inclusion was decided by consensus or by a third party when opinions differed.

1.4 Statistical Methods

Meta-analysis was performed using Stata 14.0 software. Odds ratios (OR) and 95% confidence intervals (95%CI) were used to combine effect sizes for influencing factors. Heterogeneity was assessed using I^2 test: if P>0.1 and $I^2<50\%$, indicating no significant heterogeneity, a fixed-effects model was used; if P<0.1 and $I^2>50\%$, indicating substantial heterogeneity, a random-effects model was used with sensitivity analysis or subgroup analysis. Publication bias was assessed for influencing factors included in $ $10 studies.

Results

2.1 Literature Search and Selection

A total of 46 studies were included. The initial database search yielded 12,291 relevant studies. After removing 4,376 duplicates, 7,915 studies remained. Following title and abstract screening, 469 full-text articles were reviewed, and 411 were excluded for not meeting inclusion criteria, 11 for lacking valid data, and 1 for being unavailable. The final 46 studies were included [Figure 1: see original paper].

2.2 Basic Characteristics and Quality Assessment of Included Studies

The 46 included studies had a total sample size of 8,236 cases, including 3,281 cases of cognitive impairment. We extracted 28 influencing factors including age, smoking, alcohol consumption, etc., as shown in Table 2 .

2.3 Prevalence Analysis

2.3.1 Overall Prevalence Meta-analysis of 43 cross-sectional studies showed I^2=97.1% and P<0.001, indicating substantial heterogeneity, so a random-effects model was used. The results showed that the prevalence of cognitive impairment in Chinese elderly stroke patients was 42.4% [95%CI (36.6%, 48.3%)], as shown in Figure 2 [Figure 2: see original paper].

2.3.2 Subgroup Analysis Subgroup analyses were conducted by study location and diagnostic criteria. By location: prevalence was 45.1% [95%CI (31.9%, 58.4%)] in northern China and 41.0% [95%CI (35.9%, 46.0%)] in southern China. By assessment tool: prevalence was 43.4% [95%CI (36.9%, 49.8%)] using MMSE, 50.5% [95%CI (43.6%, 57.4%)] using MoCA, and 47.9% [95%CI (43.8%, 52.1%)] using MMSE+MoCA, as shown in Table 3 .

2.3.3 Meta-regression and Sensitivity Analysis Meta-regression was performed on prevalence studies with $ 10*includedarticles*[9 − 54], *usingpublicationyear*, *studysubjects*, *studylocation*, *andassessmenttoolsascovariates*.*Nosourcesofhetero* and >2 included studies showed stable results. Meta-regression and sensitivity analysis figures are available in Appendix A (scan the QR code on the article's first page).

2.4 Influencing Factors

2.4.1 Meta-analysis of Influencing Factors Meta-analysis of 46 studies showed that female gender (OR=4.167), hypertension (OR=2.824), systolic blood pressure (OR=1.572), diabetes mellitus (OR=3.344), hyperlipidemia (OR=2.228), carotid plaque (OR=2.544), infarction location (frontal lobe: OR=1.615; temporal lobe: OR=1.739), multiple cerebral infarction (OR=2.583), encephalanalosis (OR=2.943), Hcy (OR=2.209), hyperhomocysteinemia (OR=3.043), hs-CRP (OR=4.331), and NIHSS score >10 (OR=1.977) were risk factors for cognitive impairment in Chinese elderly stroke patients (P<0.05, Table 5).

2.4.2 Meta-regression and Sensitivity Analysis Meta-regression was performed on influencing factors with $ $10 included studies [13-17,19,22-27,29-36,39,41-42,44-46,48-53], using publication year, study subjects, study location, and assessment tools as covariates. Except for diabetes mellitus, no heterogeneity sources were identified for other factors. Sensitivity analysis by sequentially removing individual studies showed stable results except for CRP, where removal of studies by Zhang Zhijian et al. [12] (P=0.205) and Ni Huafu et al. [49] (P=0.229) yielded unstable results. For diabetes mellitus, meta-regression identified study subjects (elderly cerebral infarction patients: Coef.=1.969, SE=0.722, P=0.013, 95%CI (0.458, 3.480)) and assessment tool (MoCA: Coef.=1.212, SE=0.504, P=0.027, 95%CI (0.155, 2.270)) as heterogeneity sources (P<0.05). Sensitivity analysis by sequential removal confirmed stable results for diabetes mellitus as an influencing factor. Meta-regression and sensitivity analysis figures are available in Appendix A.

2.4.3 Publication Bias Analysis Egger's test was used to assess publication bias for factors with $ $10 included studies (P<0.05 indicating publication bias). The trim-and-fill method was used to evaluate the impact of publication bias. For age (years), the OR value was <1 before trim-and-fill and >1 after, indicating substantial impact of publication bias and unstable results, as shown in Table 6 . Egger's test funnel plots and trim-and-fill funnel plots are available in Appendix A.

2.4.4 Descriptive Analysis For influencing factors that could not be pooled in meta-analysis, descriptive analysis was performed. Yang Xiaolan et al. [47] found that Enterobacter (OR=1.777, 95%CI (1.064, 2.966)) and Enterococcus

(OR=1.689, 95%CI (1.088, 2.624)) were risk factors, while Bifidobacterium (OR=0.213, 95%CI (0.085, 0.532)), Lactobacillus (OR=0.242, 95%CI (0.097, 0.603)), and Peptococcus (OR=0.409, 95%CI (0.203, 0.826)) were protective factors for cognitive dysfunction in elderly acute cerebral infarction patients ($P<0.05$). Wang Jing et al. [54] reported that serum occludin (OR=2.721, 95%CI (1.100, 6.730)) and zonula occludens-1 (ZO-1) (OR=2.824, 95%CI (1.162, 6.862)) were risk factors. Hao Chaowei et al. [43] found that collateral circulation establishment grade (OR=4.809, 95%CI (0.319, 72.558)) and quantity (OR=1.243, 95%CI (0.005, 283.568)) were risk factors for cognitive dysfunction in elderly acute cerebral infarction patients ($P<0.05$).

Discussion

3.1 Prevalence

The pooled prevalence of cognitive impairment in Chinese elderly stroke patients was 42.4% [95%CI (36.6%, 48.3%)], a relatively high level compared to the UK (22%) [63]. Our study found: (1) Higher prevalence in northern than southern China, possibly related to differences in social lifestyle, economic development, and health information access. (2) Higher prevalence when using MoCA versus MMSE. A meta-analysis showed MoCA is superior to MMSE for screening mild cognitive impairment in the elderly [64], suggesting MoCA is recommended for clinical screening of cognitive impairment in elderly stroke patients. Among included prevalence studies, specific populations showed higher rates: elderly mild cerebral infarction (76.9%) [48], first-episode cerebral infarction (60.4%) [41], acute cerebral infarction (56.8%) [40], and lacunar infarction (54.7%) [23]. These higher rates may be due to mild symptoms leading to delayed treatment, poor treatment compliance in first-episode cases, and clinical neglect of early cognitive symptoms in lacunar infarction [65]. Healthcare providers should pay more attention to early signs of cognitive impairment in these populations.

3.2 Influencing Factors

Female gender, hypertension, systolic blood pressure, diabetes mellitus, hyperlipidemia, carotid plaque, infarction location (frontal and temporal lobes), multiple cerebral infarction, encephalanalosis, Hcy, hyperhomocysteinemia, hs-CRP, and NIHSS score >10 were identified as risk factors. Women over 60 are mostly postmenopausal with decreased estrogen synthesis. Reduced estradiol levels impair cognition through interactions with basal forebrain cholinergic systems, dopamine systems, and mitochondrial bioenergetics [66]. Elderly patients with hypertension and high systolic blood pressure have impaired cerebral autoregulation, affecting brain perfusion and oxygen supply, increasing white matter lesion risk and causing cognitive decline [67]. Diabetes causes dopamine dysfunction, impairing behavioral and motor regulation [68]. Hyperlipidemia causes atherosclerosis, vascular narrowing, and promotes neurofibrillary tangles and amyloid formation [69]. Unstable carotid plaques can detach, causing cerebral ischemia and cognitive damage. The frontal cortex, especially the dorsolateral prefrontal cortex, is central to executive function; damage impairs organization, problem-solving, and planning [70]. Temporal lobe damage, particularly in the hippocampus, causes memory (delayed recall), orientation, abstraction, and calculation deficits [70]. A study of 2,950 stroke patients showed left frontotemporal infarction is closely related to post-stroke cognitive impairment [6]. Large-area infarction and encephalanalosis cause extensive cerebrovascular and neuronal damage. Hcy damages neurons through excitotoxicity, oxidative stress, vascular injury, and inhibited methylation. hs-CRP, a non-specific inflammatory marker, causes intracranial endothelial dysfunction and damages frontosubcortical vascular integrity. NIHSS score reflects neurological damage severity, with higher scores indicating worse cognitive function.

In conclusion, this study shows a 42.4% prevalence of cognitive impairment in Chinese elderly stroke patients. The identified risk factors provide targets for intervention. However, prevalence studies included broad populations, preventing subgroup analysis by study subjects—future research should conduct detailed analyses for specific populations. Age (years) showed publication bias, and CRP sensitivity analysis yielded unstable results. Factors with \$ \$2 included studies (education <6 years, physical exercise, frailty, osteoporosis, LDL-C, infarction location (occipital lobe, left hemisphere), large-area infarction, NIHSS>10, HBS-SP \$ \$55) need more research for validation. Most included studies were cross-sectional, lacking prospective designs with weaker evidence strength. Multi-center, large-sample, high-quality cohort studies are needed to further investigate influencing factors.

Author Contributions: JIAN Qiufeng was responsible for conceptualization, literature search, data extraction, statistical analysis, and manuscript writing. XU Ronghua supervised the study and provided funding support. YAO Qian revised the manuscript, controlled quality, and was responsible for overall supervision. ZHOU Yuanyuan participated in literature search and data extraction.

Conflict of Interest: The authors declare no conflict of interest.

Note: Figure translations are in progress. See original paper for figures.