Correlation Study of Cognitive Function and Its Influencing Factors in Full-Cycle Stroke Rehabilitation: Post-Print

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Date: 2024-01-11T00:00:00+00:00

Abstract

Background Post-stroke cognitive impairment (PSCI) significantly limits rehabilitation at various stages in stroke patients and leads to decreased activity participation ability and quality of life.

Objective Based on the whole-cycle rehabilitation concept for stroke, this study analyzed differences in PSCI across different ages and disease stages and their correlation with potential influencing factors through a cross-sectional study.

Methods Using simple random sampling, stroke patients were selected from the rehabilitation departments of 27 hospitals in different regions nationwide between October 2022 and July 2023 for cross-sectional analysis. A total of 402 patients were included according to the study criteria. Patients were divided into a young and middle-aged group (18-64 years) and an elderly group ($ $65 years) based on the standards of the National Bureau of Statistics of China, and into an acute phase group (1-7 days), a subacute phase group (8-180 days), and a chronic phase group (>180 days) based on the stroke recovery stages defined by the International Stroke Recovery Alliance. Baseline data were collected through interviews, assessments, and electronic medical record systems. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA), and scores for each cognitive domain and total scale score were calculated. The patients' disease status and physical function were assessed using the National Institutes of Health Stroke Scale (NIHSS), Fugl-Meyer Assessment-Upper Extremity (FMA-UE), Fugl-Meyer Assessment-Lower Extremity (FMA-LE), Berg Balance Scale (BBS), Modified Barthel Index (MBI), Hospital Anxiety and Depression Scale-Anxiety (HADS-A), and Hospital Anxiety and Depression Scale-Depression (HADS-D). Spearman rank correlation analysis was used to explore the correlation between cognitive function levels and other clinical indicators across different ages and disease stages.

Results The prevalence of PSCI among stroke patients was 76.4% (307/402), with a prevalence of 81.0% (136/168) in elderly patients and 73.1% (171/234) in young and middle-aged patients. The prevalence was 56% (14/25) in the acute phase, 78.4% (265/338) in the subacute phase, and 71.8% (28/39) in the chronic phase. Results from age and disease stage grouping showed that elderly patients had lower scores in visuospatial and executive function, attention, calculation, delayed recall, and total MoCA score compared with the young and middle-aged group ($P<0.05$). Subacute phase patients had lower scores in visuospatial and executive function, language, delayed recall, and total MoCA score compared with the acute phase group ($P<0.05$). Correlation analysis revealed that total MoCA score was positively correlated with education level (rs=0.314), stroke type (rs=0.114), FMA-UE (rs=0.245), FMA-LE (rs=0.242), BBS (rs=0.265), and MBI (rs=0.293) ($P<0.001$), and negatively correlated with gender (rs=-0.107), age (rs=-0.103), history of hypertension (rs=-0.112), hemiplegic side (rs=-0.139), disease course (rs=-0.135), NIHSS (rs=-0.107), HADS-A (rs=-0.239), and HADS-D (rs=-0.280) ($P<0.05$). Further stratified analysis showed that in both the young and middle-aged and elderly groups, education level, NIHSS, and physical function indicators including FMA-UE, FMA-LE, BBS, MBI, HADS-A, and HADS-D were correlated with total MoCA score ($P<0.05$). In acute phase patients, disease course, FMA-UE, and HADS-A were correlated with total MoCA score ($P<0.05$). In subacute phase patients, age, education level, hypertension, alcohol consumption history, stroke type, hemiplegic side, disease course, NIHSS, and physical function indicators including FMA-UE, FMA-LE, BBS, MBI, HADS-A, and HADS-D were correlated with total MoCA score ($P<0.05$). In chronic phase stroke patients, education level, hypertension, and HADS-D were correlated with total MoCA score ($P<0.05$).

Conclusion PSCI is closely associated with age, disease stage, education level, motor function, balance ability, activities of daily living, and anxiety and depression levels in stroke patients. Personalized prevention strategies and intervention plans should be developed for patients based on different stratifications of potential cognitive influencing factors, and screening and attention for cognition should be enhanced from early disease stages through later rehabilitation phases.

Full Text

Correlation Study of Cognitive Function and Its Influencing Factors from the Perspective of Full-Cycle Rehabilitation in Stroke

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Abstract

Background: Post-stroke cognitive impairment (PSCI) significantly limits recovery at all stages and leads to declines in activity participation and quality of life. **Objective:** Based on the concept of full-cycle rehabilitation in stroke, this cross-sectional study analyzes differences in PSCI across different ages and disease stages and examines correlations with potential influencing factors. **Methods:** Using simple random sampling, stroke patients hospitalized in rehabilitation departments across 27 hospitals in different regions of China were recruited from October 2022 to July 2023 for cross-sectional analysis. A total of 402 patients were included according to study criteria and categorized into young and middle-aged group (18-64 years) and elderly group ($ $65 years) based on National Bureau of Statistics standards, and into acute-phase (1-7 days), subacute-phase (8-180 days), and chronic-phase (>180 days) groups based on International Stroke Rehabilitation Alliance definitions. Baseline data were collected through interviews, assessments, and electronic medical record systems. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA), with subscale and total scores calculated. Disease status and physical function were assessed using the National Institutes of Health Stroke Scale (NIHSS), Fugl-Meyer Assessment-Upper Extremity (FMA-UE), Fugl-Meyer Assessment-Lower Extremity (FMA-LE), Berg Balance Scale (BBS), Modified Barthel Index (MBI), Hospital Anxiety and Depression Scale-Anxiety (HADS-A), and Hospital Anxiety and Depression Scale-Depression (HADS-D). Spearman rank correlation analysis was used to explore relationships between cognitive function levels and other clinical indicators across different ages and disease stages. **Results:** The prevalence of PSCI was 76.4% (307/402), with 81.0% (136/168) in elderly patients and 73.1% (171/234) in young and middle-aged patients. By disease stage, prevalence was 56% (14/25) in acute phase, 78.4% (265/338) in subacute phase, and 71.8% (28/39) in chronic phase. Group comparisons showed elderly patients had lower scores in visuospatial/executive function, attention, calculation, delayed recall, and total MoCA than young/middle-aged patients ($P<0.05$). Subacute-phase patients had lower scores in visuospatial/executive function, language, delayed recall, and total MoCA than acute-phase patients ($P<0.05$). Correlation analysis revealed total MoCA score was positively correlated with education level (r =0.314), stroke type (r =0.114), FMA-UE (r =0.245), FMA-LE (r =0.242), BBS (r =0.265), and MBI (r =0.293) (P<0.001), and negatively correlated with gender (r =-0.107), age (r =-0.103), hypertension history (r =-0.112), hemiplegic side (r =-0.139), disease duration (r =-0.135), NIHSS (r =-0.107), HADS-A (r =-0.239), and HADS-D (r =-0.280) (P<0.05). Stratified analyses showed both age groups demonstrated correlations between MoCA total score and education level, NIHSS, and physical function indicators including FMA-UE, FMA-LE, BBS, MBI, HADS-A, and HADS-D (P<0.05). In acute-phase patients, disease duration, FMA-UE, and HADS-A correlated with MoCA total score (P<0.05). In subacute-phase patients, age, education level, hypertension, alcohol consumption history, stroke type, hemiplegic side, disease duration, NIHSS, and all physical function indicators correlated with MoCA total score (P<0.05). In chronic-phase patients, only education level, hypertension, and HADS-D correlated with MoCA total score (P<0.05). **Conclusion:** PSCI is closely associated with age, disease stage, education level, motor function, balance, activities of daily living, and anxiety/depression levels. Personalized prevention strategies and intervention protocols should be developed based on stratified cognitive risk factors, with enhanced cognitive screening and attention from early disease stages through late rehabilitation phases.

Keywords: Stroke; Cognitive function; Full-cycle; Rehabilitation; Multicenter study; Cross-sectional study; Influencing factor analysis; Spearman rank correlation analysis

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Introduction

Stroke reportedly increases the risk of cognitive impairment by at least 26-27 times [1]. Post-stroke cognitive impairment (PSCI) refers to all forms of cognitive decline occurring within 3-6 months after stroke [2-3]. Studies indicate PSCI prevalence ranges from 13.6% to 80.0% [4]. PSCI profoundly affects patients' rehabilitation progress, activity participation, and recovery of other physical functions [5], posing significant clinical challenges that have become a research priority. Compared with disease status and other physical dysfunctions, cognitive issues are often overlooked and may not receive adequate attention even in acute stroke clinical care [6].

Full-cycle stroke rehabilitation encompasses four dimensions: the entire disease cycle, hierarchical diagnosis and treatment cycle, full participation of personnel, and geographic coverage [7]. Cognitive rehabilitation has distinct characteristics at different stages, and targeted, stratified interventions for PSCI patients can better improve cognitive function and rehabilitation efficiency [8-9]. Although prospective studies have identified multiple PSCI risk factors [10-12], results remain contradictory, and research on cognitive correlates specific to age and disease stage is lacking. Therefore, this study, grounded in the full-cycle rehabilitation concept, conducts a cross-sectional analysis of stroke patients to explore cognitive function differences and potential influencing factors across age groups and disease stages, providing references for clinical treatment and future research.

Methods

Study Design and Participants This multicenter cross-sectional study recruited stroke patients hospitalized in rehabilitation departments across 27 hospitals in 8 provinces from October 2022 to July 2023. Participating institutions included Huashan Hospital affiliated with Fudan University, Shanghai Jing'an District Central Hospital, Pudong Hospital affiliated with Fudan University, Shanghai Third Rehabilitation Hospital, the First Affiliated Hospital of Fujian Medical University, National Regional Medical Center, Rehabilitation Hospital affiliated with Fujian University of Traditional Chinese Medicine, Longyan Traditional Chinese Medicine Hospital, Fujian Provincial Hospital, Xiamen Hospital of Zhongshan Hospital affiliated with Fudan University, Quanzhou First Hospital, Fuding Hospital, Nanping First Hospital affiliated with Fujian Medical University, Xiamen International Trade Taihe Rehabilitation Hospital, Second Hospital of Sanming City, Changle District Hospital of Fuzhou, Yongchun County Hospital, Dehua County Hospital, Jianyang First Hospital, Affiliated Hospital of Putian University, First Hospital of Fuzhou, General Hospital of Ningxia Medical University, Beijing Tiantan Hospital affiliated with Capital Medical University, Shenzhen Longhua District Central Hospital, Second Affiliated Hospital of Kunming Medical University, Second Affiliated Hospital of Chongqing Medical University, and Third Clinical Medical College of Changchun University of Traditional Chinese Medicine.

Inclusion criteria were: (1) diagnosis of cerebral hemorrhage or cerebral infarction according to the 2019 Diagnostic Criteria for Major Cerebrovascular Diseases in China; (2) first onset with disease duration within 1 year (1-365 days); (3) age >18 years; (4) stable vital signs enabling completion of routine post-stroke rehabilitation assessments; and (5) signed informed consent. **Exclusion criteria** were: (1) conditions where movement might exacerbate or cause adverse effects (e.g., recurrent stroke, falls, fractures); (2) psychological disorders preventing assessment; and (3) inability to sign informed consent.

Using simple random sampling, 437 patients were initially recruited. After excluding 10 with incomplete baseline information, 18 lacking cognitive assessment scores, and 7 missing other functional assessment data, 402 participants were finally included. The study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No.: 闽医大附一伦理医研 [2022]280 号), with all participants or their proxies providing informed consent.

Assessment Tools A self-designed questionnaire collected baseline data through interviews and electronic medical record review, including gender, age, education level, handedness, comorbidities (hypertension, coronary heart disease, diabetes), lifestyle factors (smoking, alcohol consumption), stroke type (cerebral hemorrhage, cerebral infarction, both), hemiplegic side, and disease duration. Smoking history was defined as $ $3 years of smoking with average daily consumption $ $3 cigarettes; alcohol consumption history was defined as average daily intake $ $2 standard drinks.

Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) [13], which comprises 12 tests covering 7 domains: visuospatial/executive function, attention, calculation, language, abstract thinking, memory, and orientation. Total score ranges from 0-30, with higher scores indicating better cognitive ability; scores <26 indicate cognitive impairment [14].

Disease status and physical function were evaluated by uniformly trained assessors using standardized protocols, including one disease status measure and five physical function assessments: (1) National Institutes of Health Stroke Scale (NIHSS) to quantify stroke severity (range 0-42, higher scores indicating greater neurological deficit); (2) Fugl-Meyer Assessment (FMA) for upper and lower extremity motor function, with Fugl-Meyer Assessment-Upper Extremity (FMA-UE) [15] containing 33 items (total score 66) and Fugl-Meyer Assessment-Lower Extremity (FMA-LE) containing 17 items (total score 34), where higher scores indicate better function; (3) Berg Balance Scale (BBS) for balance function (14 items, range 0-56, higher scores indicating better balance); (4) Modified Barthel Index (MBI) for activities of daily living (11 items, maximum score 100, higher scores indicating greater independence); and (5) Hospital Anxiety and Depression Scale (HADS) for anxiety and depression severity, including HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D) subscales (7 items each, 14 total, higher scores indicating more severe symptoms).

Grouping Based on National Bureau of Statistics age classification standards [16], patients were divided into young/middle-aged (18-64 years) and elderly ($ $65 years) groups. According to International Stroke Rehabilitation Alliance definitions [17], patients were categorized by disease duration into acute-phase (1-7 days), subacute-phase (8-180 days), and chronic-phase (>180 days) groups to analyze relationships between cognitive function and general characteristics, disease severity, and other physical functions.

Statistical Methods As a cross-sectional study, sample size was calculated using PASS 15 based on previous literature reporting 53.1% PSCI incidence [18], with two-sided α=0.05, allowable error of 5.5%, yielding N=332. Considering 15% attrition, at least 382 patients were required. With 437 participants enrolled, the sample size requirement was met. Data were organized in Excel, and after excluding invalid data, SPSS 25.0 was used for analysis. Categorical data were described using frequencies and percentages, with between-group comparisons using ^{2} tests. Normally distributed continuous data were expressed as ($\bar{x}\pm s$) and compared using independent samples t-tests or one-way ANOVA.

Non-normally distributed data were described as M(P_{25},P_{75}) and compared using Mann-Whitney U or Kruskal-Wallis H tests. Spearman rank correlation analysis examined relationships between cognitive function and other clinical indicators. Statistical significance was set at P<0.05.

Results

Participant Characteristics Among 402 patients from 17 hospitals in one province and 10 hospitals across 7 other provinces, ages ranged from 22-87 years (mean 60.6$±$11.8 years), with 296 males (73.6%) and 106 females (26.4%). Right-handedness was present in 372 cases (92.5%) and left-handedness in 30 (7.5%). Education level was primary school or below in 157 cases (39.1%), with 349 patients (86.8%) having $ *12yearsofeducation.Comorbiditiesincludedhypertensionin*211(52.5±$78.9 days). Hemiplegic side was left in 209 cases (52.0%) and right in 193 (48.0%).

Prevalence of PSCI Overall, 307 patients had cognitive impairment, yielding a prevalence of 76.4%. PSCI prevalence differed significantly by education level and disease stage (P<0.05) but not by gender, age group, or stroke type (P>0.05) .

Cognitive Differences Across Age and Disease Stage Elderly patients had significantly lower scores than young/middle-aged patients in visuospatial/executive function, attention, calculation, delayed recall, and total MoCA (P<0.05), with no significant differences in language, abstract thinking, or orientation (P>0.05) .

Comparisons across acute, subacute, and chronic phases revealed significant differences in visuospatial/executive function, language, delayed recall, and total MoCA (P<0.05), but not in attention, calculation, abstract thinking, or orientation (P>0.05). Subacute-phase patients scored lower than acute-phase patients in visuospatial/executive function, language, delayed recall, and total MoCA (P<0.05) .

Correlations Between Cognitive Function and Potential Influencing Factors Total MoCA score correlated positively with education level (r =0.314), stroke type (r =0.114), FMA-UE (r =0.245), FMA-LE (r =0.242), BBS (r =0.265), and MBI (r =0.293) (P<0.001), and negatively with gender (r =-0.107), age (r =-0.103), hypertension history (r =-0.112), hemiplegic side (r =-0.139), disease duration (r =-0.135), NIHSS (r =-0.107), HADS-A (r =-0.239), and HADS-D (r =-0.280) (P<0.05). Handedness, coronary heart disease, diabetes, and smoking history showed no significant correlation with MoCA total score .

Stratified Analyses by Age and Disease Stage In both age groups, education level, NIHSS, and physical function indicators (FMA-UE, FMA-LE, BBS, MBI, HADS-A, HADS-D) correlated with MoCA total score (P<0.05). In acute-phase patients, disease duration, FMA-UE, and HADS-A correlated with MoCA total score (P<0.05). In subacute-phase patients, age, education level, hypertension, alcohol consumption history, stroke type, hemiplegic side, disease duration, NIHSS, and all physical function indicators correlated with MoCA total score (P<0.05). In chronic-phase patients, only education level, hypertension, and HADS-D correlated with MoCA total score (P<0.05) [TABLE:5, TABLE:6].

Discussion

This study found PSCI prevalence of 76.4% among stroke patients, higher than the 53.1% reported in previous literature [18], possibly due to inclusion of rehabilitation inpatients with more severe functional impairments requiring intensive therapy. Prevalence decreased with higher education levels. Acute-phase prevalence was significantly lower than subacute and chronic phases, while chronic-phase prevalence was slightly lower than subacute phase, consistent with findings that PSCI incidence increases over time post-stroke [23] but may be influenced by pre-stroke cognitive status [24].

Our correlation analysis identified associations between PSCI and gender, age, education, hypertension, alcohol consumption history, stroke type, hemiplegic side, disease duration, and stroke severity, aligning with previous research [25-27]. Notably, hemiplegic side showed negative correlation with cognitive function, indicating worse cognition in left hemisphere lesions, consistent with BOUTROS et al.'s multicenter longitudinal study [28]. This likely reflects left hemisphere dominance for language, which is required for most neuropsychological tests. Left hemisphere stroke increases dementia risk nearly threefold compared to right hemisphere lesions [27], with left frontotemporal and thalamic infarcts closely associated with PSCI [29-30].

Stroke type positively correlated with cognitive function, suggesting worse cognition after cerebral hemorrhage than infarction—a finding contrasting with some studies but supported by recent research [27]. This discrepancy may stem from differences in underlying conditions, genetic factors, brain injury extent, and comorbidities, warranting larger prospective cohort studies.

Cognitive function correlated with motor function, balance, and activities of daily living, consistent with a prospective multicenter study of 567 stroke patients showing associations between motor capacity and global cognitive impairment [31]. Anxiety and depression showed negative correlations with cognition, supporting research indicating that timely post-stroke antidepressant treatment may improve physical and cognitive recovery [33] and that post-stroke anxiety correlates with cognitive decline [34]. While WILLIAMS et al. [35] reported that the association between PSCI and anxiety was mediated by depression, our findings align with the overall literature.

Advanced age increases PSCI risk [11]. Our age-stratified analysis revealed that elderly patients ($ $65 years) performed significantly worse than young/middle-aged adults in visuospatial/executive function, attention, calculation, and overall cognition. Further stratified analysis showed stronger correlations between cognition and motor/balance/daily living functions in young/middle-aged patients, while anxiety/depression showed stronger cognitive correlations in elderly patients. A 12-month randomized controlled trial demonstrated that exercise training improves cognition in chronic stroke [36], and high-intensity interval training may promote neuroplasticity and cognitive function [37], consistent with our findings that motor, coordination, and balance performance requires executive function participation [38]. Therefore, community and home-based mobility may be particularly challenging for elderly PSCI patients with higher fall risk, necessitating greater attention to cognitive, physical, emotional, and functional independence aspects in community rehabilitation.

Our findings also revealed that subacute-phase patients had significantly lower visuospatial/executive function, language, memory, and overall cognition than acute-phase patients. Acute tissue damage may affect cognition and increase impairment risk [5], while subacute patients show domain-specific cognitive abnormalities [39]. HOBDEN et al. [40] found that cortical atrophy severity correlates with post-stroke cognition, with subacute-phase atrophy more strongly associated with global and domain-specific cognition than acute-phase atrophy, possibly due to more pronounced cortical atrophy compared to acute stages. A prospective multicenter study of 666 ischemic and hemorrhagic stroke patients found small vessel disease correlated with cognitive impairment in executive function, attention, language, and visuospatial abilities, with significant decline at 6- and 12-month follow-ups [41], consistent with our results.

Correlation analyses confirmed that subacute-phase cognition significantly correlated with motor, balance, quality of life, anxiety, and depression—aligning with our overall findings—while acute and chronic phases showed fewer such correlations. Previous studies reported that persistent cognitive impairment in acute and chronic phases increased risk of poor physical function outcomes [42-43]. The discrepancy may stem from our sample composition, with 84.1% subacute-phase patients potentially biasing results. The negative correlation between cognition and disease duration in acute and subacute phases suggests cognitive impairment worsens within six months post-stroke, possibly due to extensive white matter microstructural damage in corpus callosum, internal capsule anterior limb, and left superior corona radiata in subacute PSCI patients [44], with persistent white matter damage affecting cognitive recovery over time [45].

Limitations This study has several limitations. First, it included only rehabilitation inpatients from certain regions, lacking outpatient and community hospital data, which may limit generalizability to the broader stroke population across China. Second, as a cross-sectional study, we identified correlations but cannot establish causality between cognitive function and other indicators, requiring confirmation through large-scale, multicenter prospective cohort studies. Third, reliance on scale assessments and baseline surveys limits predictive value; future studies should incorporate more objective measures such as neuroimaging and laboratory tests combined with lesion location and severity analyses to uncover additional insights.

Conclusion

Lower education level was associated with higher PSCI prevalence. Subacute-phase patients showed higher PSCI prevalence than chronic-phase patients, who in turn had higher prevalence than acute-phase patients. Post-stroke cognitive function negatively correlated with gender, age, hypertension history, hemiplegic side, disease duration, and NIHSS, and positively correlated with alcohol consumption history and stroke type. Stroke severity, motor function, activities of daily living, and anxiety/depression levels correlated with PSCI, particularly among elderly patients and in the subacute phase. Negative correlations between disease duration and cognition in acute and subacute phases underscore the need for early and continuous cognitive monitoring, timely intervention, and follow-up in clinical and community rehabilitation settings to promote functional improvement and accelerate recovery. This study explores potential factors influencing cognitive impairment across ages and disease stages, providing valuable references for prevention strategies and personalized interventions, while guiding future research directions.

Author Contributions

TU Shuting was responsible for study design, implementation, statistical analysis, and manuscript writing. LIN Jiaying, ZHUANG Jinyang, XIANG Jingnan, WEI Dongshuai, and XIE Yong conducted investigations, assessments, and data collection. JIA Jie supervised manuscript quality control and revision, and was accountable for the overall work.

Conflict of Interest: None declared.

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Received: October 12, 2023; Revised: December 12, 2023
Edited by: MAO Yamin

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