

The association of different types of cerebral infarction with post-stroke depression and cognitive impairment

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Abstract

The aim of this study was to investigate post-stroke depression (PSD) and cognitive impairments in patients with different types of cerebral infarction.

A total of 110 patients with cerebral infarction treated in our hospital from January 2015 to February 2016 were included in present study. Forty-seven patients were PSD patients and 63 patients were non-PSD patients. The Hamilton Depression Rating Scale (HAMD) and Mini-Mental State Examination (MMSE) were employed to assess depression and cognition of patients

Among PSD patients, the proportion of patients with partial anterior circulation infarction (PACI, 68.75%) was significantly higher than patients with lacunar circulation infarction (LACI, 29.17%) and posterior circulation infarction (POCI, 26.67%) ($P < .05$). No significant difference was found in PSD patients with LACI and POCI ($P > .05$). The MMSE score of patients with PACI (18.05 ± 2.61) was lower than patients with POCI and LACI ($P < .05$), however, no significant difference was found in patients with LACI and POCI ($P > 0.05$). The incidences of cognitive impairment in patients with PACI, LACI, and POCI were 12.50%, 14.58%, and 13.33%, respectively. The MMSE score of PSD patients (21.23 ± 2.12) was significantly lower than non-PSD patients ($P < .05$).

Compared with LACI and POCI patients, PACI patients had a higher incidence of PSD and impaired cognitive functions. In addition, affective disorders such as depression may be correlated with cognitive impairment in patients with cerebral infarction.

Abbreviations: ANOVA = analysis of variance, HAMD = Hamilton Depression Rating Scale, LACI = lacunar circulation infarction, LCSPT = limbic-cortical-striatal-pallidal-thalamic, MMSE = Mini-Mental State Examination, OCSPT = Oxfordshire Community Stroke Project, PACI = partial anterior circulation infarction, POCI = posterior circulation infarction, PSD = post-stroke depression.

Keywords: cerebral infarction, cognitive dysfunction, depression

1. Introduction

Post-stroke depression (PSD) has been recognized as a common sequela of stroke, with an increased morbidity and mortality.^[1] Approximately 85% of patients with strokes had PSD,^[2] which led to more serious dysfunctions.^[3] The latest meta-analysis of 61 cohort studies including 25,488 patients demonstrated that 31% of patients developed into depression at any time point up to 5 years following stroke.^[4] Furthermore, lesion locations have been extensively investigated as a risk factor for PSD. Although numerous studies have focused on the association between the presence or absence of PSD and lesion locations of stroke, the clinical association remains unclear.^[2] The relationship between PSD and cognitive impairment (especially executive dysfunction) has been well-established.^[5] Initial studies have demonstrated that stroke patients with major depression had significantly lower

Mini-Mental State Examination (MMSE) scores, compared with patients without depression who were matched for both lesion locations and lesion volumes with patients of PSD.^[6] Shared pathophysiologic mechanisms seem to exist between cognitive impairments and cerebrovascular diseases.^[7] In addition, it has been well-established that stroke itself increases the risk of cognitive impairments in the future.^[8] Cerebral infarction is an important part of stroke, and the incidence of cerebral infarction is 3.4/100,000 to 11.3/100,000 in patients under 45 years of age.^[9,10] Cerebral infarction increases the incidence of PSD and cognitive impairments, as well as mortality, which has become a common and acute disease in the Neurology Department of hospitals. With the development of medical science, the medical mode has gradually transformed from the biological mode into the combined mode based on biology, society, and psychology.^[11] Therefore, the concern for life and health of stroke patients not only focuses on the recovery of limb function but also on nonlimb dysfunction.^[12] However, no traditional clinical studies have focused on this topic. Therefore, it is important to investigate the association of different types of cerebral infarction with PSD and cognitive dysfunction, providing more evidences for clinical treatment strategies. The incidence of PSD, the MMSE scores of patients with different types of cerebral infarction, and the MMSE scores of PSD and non-PSD patients were compared in present study.

2. Methods

2.1. Subjects

A total of 110 patients with cerebral infarction treated in our hospital from January 2015 to February 2016 were included in

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the study. Inclusion criteria included patients who met the diagnostic criteria established at the Fourth National Cerebrovascular Disease Conference of China, patients who had cerebral infarction less than 2 weeks, patients with comprehensive imaging data, and patients with a signed informed consent. Exclusion criteria included patients with the history of brain diseases, other serious somatic diseases, and mental diseases; patients with severe aphasia and unconsciousness, and hardly to cooperate during the examination; patients with liver and kidney dysfunctions, Parkinson disease, multiple sclerosis, and other known diseases that may lead to cognitive impairments; and patients with serious heart, lung dysfunctions, and other functional damages. All subjects received conventional treatments with aspirin, atorvastatin, and citicoline. The study was approved by the medical ethics committee of Aerospace Center Hospital and all subjects had given the informed consent.

In the study, 47 patients suffered from PSD, while 63 patients did not have PSD. Twenty-eight PSD patients were male and 19 were female, whose age ranged from 46 to 63 years (Mean: 57.22). The average education duration was 8.14 years. Thirty-nine patients without PSD were male and 24 were female, whose age ranged from 43 to 65 years (Mean: 56.43). The average education duration was 8.6 years. No significant differences were found in gender, age, and education duration between PSD patients and non-PSD patients ($P > .05$).

2.2. Material and procedure

All patients were assessed by Hamilton Depression Rating Scale, 17-item (HAMD-17) and MMSE within 2 weeks after the onset of cerebral infarction. The total score of HAMD-17 with more than 7 was considered as depression. Patients who met the following criteria were considered having cognitive dysfunctions: patients with the education level of junior high school or above, had the MMSE score ≤ 24 , patients with the educational level of primary school had the MMSE score ≤ 20 , or illiterate patients had the MMSE score ≤ 17 .^[13,14]

The stroke types were determined according to the Oxford shire Community Stroke Project (OCSP) classification system.^[15] In the study, 32 patients with cerebral infarction had partial anterior circulation infarction (PACI), 48 patients had lacunar circulation infarction (LACI), and 30 patients had posterior circulation infarction (POCI). No significant differences were found in gender, age, and educational level of patients with PACI, LACI, and POCI ($P > .05$, see Table 1).

2.3. Statistical analysis

SPSS 19.0 statistical software was employed for the statistical analysis in the study. Categorical variables were displayed in n (%), while continuous variables were displayed in mean \pm standard deviation ($\bar{x} \pm SD$). Chi-square test (χ^2 test) was used to

Table 2
Comparison of PSD in PACI, LACI, and POCI.

Cerebral infarction type	No.	PSD (n, %)	χ^2	P
PACI	32	22 (68.75)*	15.59	< .05
LACI	48	14 (29.17)		
POCI	30	8 (26.67)		

LACI = lacunar circulation infarction, PACI = partial anterior circulation infarction, POCI = posterior circulation infarction.

* Compared with other types, $P < .05$.

Table 3
Comparison of MMSE scores in patients with PACI, LACI, and POCI.

Cerebral infarction type	No.	MMSE score ($\bar{x} \pm SD$)	F	P
PACI	29	18.05 \pm 2.61*	2.16	> .05
LACI	47	24.26 \pm 3.10		
POCI	30	25.32 \pm 2.79		

LACI = lacunar circulation infarction, PACI = partial anterior circulation infarction, POCI = posterior circulation infarction.

* Compared with other types, $P < .05$.

test differences in gender and the prevalence of PSD in patients with PACI, LACI, and POCI. One-way analysis of variance (ANOVA) was used to compare differences of MMSE scores in patients with PACI, LACI, and POCI, and the correction method for post hoc test was Bonferroni. Independent-sample *t* test was used to assess differences of MMSE scores in patients with or without PSD. $P < .05$ was considered a statistical significance.

3. Results

3.1. The prevalence of PSD in patients with PACI, LACI, and POCI

The prevalence of PSD was significantly higher in patients with PACI (68.75%) than patients with LACI and POCI ($P < .05$). No significant differences were found in the prevalence of PSD in patients with LACI and POCI ($P > .05$, see Table 2).

3.2. MMSE scores of patients with PACI, LACI, and POCI

The MMSE score was significantly lower in PACI patients (18.05 \pm 2.61) than LACI and POCI patients ($P < .05$). The difference in MMSE scores between patients with LACI and POCI was not statistically significant ($P > .05$, see Table 3). The prevalence of cognitive impairment was 13.79% in PACI patients, 14.89% in LACI patients, and 13.33% in POCI patients. And there were no significant differences in the prevalence of cognitive impairments in PACI, LACI, and POCI groups.

Table 1
Demographic variables of patients with PACI, LACI, and POCI.

n/ $\bar{x} \pm SD$	PACI (n=32)	LACI (n=48)	POCI (n=30)	F/χ^2	P
Male/Female	20/12	27/21	20/10	0.889	> .05
Age, y	57.81 \pm 9.21	56.04 \pm 9.21	57.44 \pm 9.21	1.322	> .05
Educational level, y	8.131 \pm 9.2	8.734 \pm 9.2	8.514 \pm 9.2	2.014	> .05

LACI = lacunar circulation infarction, PACI = partial anterior circulation infarction, POCI = posterior circulation infarction.

Table 4**Comparison of MMSE scores between PSD and non-PSD patients.**

Patient types	No.	MMSE score ($\bar{x} \pm SD$)	t	P
PSD	46	21.23 \pm 2.12	25.42	< .05
Non-PSD	60	24.62 \pm 3.01		

PSD = post-stroke depression.

3.3. Comparison of MMSE scores between PSD and non-PSD patients

The MMSE score was lower in PSD patients (21.23 \pm 2.12) than non-PSD patients, and the difference was statistically significant ($P < .05$, see Table 4).

4. Discussion

Our study found that among PSD patients, the proportion of PACI patients was significantly higher than patients with LACI and POCI. Furthermore, the MMSE score of patients with PACI was lower than patients with POCI and LACI. MMSE scores of PSD patients were significantly lower than non-PSD patients. Many studies have revealed that types of cerebral infarction may be related to PSD and cognitive impairments and may also interact with each other.^[16]

PSD is a common complication of stroke, which seriously affects the recovery of mental, language, and cognitive functions of patients. Besides, the incidence of cognitive impairments after stroke is relatively high, which generally manifests as language, attention, understanding, calculation, and memory impairment, and aggravates with the increase in age of patients.^[17] As a component of stroke, cerebral infarction is also the key reason for the high fatality rate of stroke. Cerebral infarction seriously affects the quality of life and recovery of patients and increases the incidence of depression and cognitive impairments. After analyzing hundreds of patients with cerebral infarction, Chen et al^[18] found the independent risk factor of PSD, that is, frontal lobe lesions in the brain. Terroni et al^[19] demonstrated that larger lesions in the left cortical regions of the limbic-cortical-striatal-pallidal-thalamic circuit were associated with a higher incidence of depression. They also found that depression was associated with larger lesions in areas of the medial prefrontal cortex, including the ventral and dorsal anterior cingulate cortex, subgenual cortex, the subiculum, and amygdala.^[19] PACI is a type of cerebral infarction affecting part of the anterior circulation supplying 1 side of the brain. The possible interpretation of differences between patients of PACI, LACI and POCI in PSD and cognitive functions is that PACI might involve more lesions in those brain areas. Anterior circulation infarction induces more serious injuries in PACI, compared with LACI and POCI. Patients with anterior circulation infarction have greater levels of depression and more severe cognitive impairment.^[20] Therefore, these different types of cerebral infarction are closely associated with PSD and cognitive impairment, which needs to be further studied.

Although the differences in the prevalence of cognitive impairment among the 3 types of cerebral infarction were not statistically significant, patients with PACI had lower MMSE scores for cognitive impairment. This suggested that the incidence of cognitive impairment in patients with different types of cerebral infarction was the same. However, the severity of cognitive impairment was significantly higher in patients with

PACI than patients with LACI and POCI.^[21] In terms of solely PSD, the MMSE score was lower in PSD patients than non-PSD patients, and the difference was statistically significant. This further revealed the relationship between PSD and cognitive impairment, in which PSD would reduce the cognitive function of patients.^[22]

However, there were some limitations in our study. First, in this study, we did not consider the impact of the sex difference on the results because of the limited samples. As previous studies showed that sex may influence the incidence of PSD in stroke patients^[23], sex should be considered in the future study. Second, in the study, we employed MMSE as the measurement of general cognitive functions rather than montreal cognitive assessment, Alzheimer's disease assessment scale-cognitive subscale, or Addenbrooke's cognitive examination-revised-R, etc. More studies should be conducted using other assessment tools of cognitions to verify our results. Third, in this study, we did not perform other objective assessments, such as functional magnetic resonance imaging or genetics. Further studies should explore possible mechanisms to make interpretations more firmed.

In summary, the incidence of PSD is higher and cognitive impairment is more pronounced in patients with PACI, than in patients with LACI and POCI. Depressive disorder may be correlated with cognitive impairment in patients with cerebral infarction. This may provide a theoretical basis for clinical studies.

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References

- Williams LS, Ghose SS, Swindle RW. Depression and other mental health diagnoses increase mortality risk after ischemic stroke. *Am J Psychiatry* 2004;161:1090–5.
- Robinson RG, Jorge RE. Post-stroke depression: a review. *Am J Psychiatry* 2016;173:221–31.
- Cully JA, Gfeller JD, Heise RA, et al. Geriatric depression, medical diagnosis, and functional recovery during acute rehabilitation. *Arch Phys Med Rehab* 2005;86:2256–60.
- Hackett ML, Pickles K. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *Int J Stroke* 2014;9:1017–25.
- Robinson RG. *The Clinical Neuropsychiatry of Stroke*. 2nd ed. 2006; Cambridge University Press, New York:p 470.
- Starkstein SE, Robinson RG, Price TR. Comparison of patients with and without post-stroke major depression matched for size and location of lesion. *Arch Gen Psychiatry* 1988;45:247–52.
- Kalaria RN. Linking cerebrovascular defense mechanisms in brain ageing and Alzheimer's disease. *Neurobiol Aging* 2009;30:1512–4.
- Dregan A, Wolfe CD, Gulliford MC. Does the influence of stroke on dementia vary by different levels of pre-stroke cognitive functioning? A cohort study. *Stroke* 2013;44:3445–51.
- Guidetti D, Baratti M, Zucco RG, et al. Incidence of stroke in young adults in the Reggio Emilia area, northern Italy. *Neuroepidemiology* 1993;12:82–7.

- [10] Kristensen B, Malm J, Carlberg B, et al. Epidemiology and etiology of ischemic stroke in young adults and 18 to 44 years in Northern Sweden. *Stroke* 1997;28:1702–9.
- [11] Wang GF. Discussion on the change of primary medical model from the rehabilitation treatment of stroke patients. *Ji Ceng Yi Xue Lun Tan* 2015;3:2155–6.
- [12] Yan WJ, Dai XN, Liu J, et al. Application of rehabilitation nursing assessment in the guidance of limb function task-oriented training for stroke patients. *Nurs J Chin People Liberat Army* 2014;31:71–3.
- [13] Shen DC, Wang ZX, Xiao FL, et al. Scientific statement of inclusion and exclusion criteria for intravenous use of acute ischemic stroke (second part) statement of health professionals from the American Heart Association /American Stroke Association. *Chin J Stroke* 2016;11:226–8.
- [14] Powers WJ, Derdeyn CP, Biller J, et al. American Heart Association Stroke Council 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American H. *Stroke* 2015;46:3020–35.
- [15] Andersen G, Vestergaard K, Ingemann-Nielsen M, et al. Risk factors for post-stroke depression. *Acta Psychiatr Scand* 1995;92:193–8.
- [16] Burke Quinlan E, Dodakian L, See J, et al. Neural function, injury, and stroke subtype predict treatment gains after stroke. *Ann Neurol* 2015;77:132–45.
- [17] Cui SQ, Ren MX, Du YH, et al. Effect of computer assisted training on cognitive impairment after stroke. *Chin J Clin Res* 2014;27:21–3.
- [18] Chen YJ, Li JS, Sun Q. Analysis of pathogenic bacteria and risk factors of pulmonary infection in patients with acute stroke. *Chin J Nosocomiol* 2014;24:1407–9.
- [19] Terroni L, Amaro E, osifescu DV, et al. Stroke lesion in cortical neural circuits and post-stroke incidence of major depressive episode: a 4-month prospective study. *World J Biol Psychiatry* 2011;12:539–48.
- [20] Li ZL, Wu HF. The effect of serum level of serum in the treatment of ischemic stroke patients with depression. *J Hainan Med Coll* 2015;21:262–4.
- [21] Wan QR, Hu YR, Liu H, et al. Effect of early prevention of post-stroke depression on functional rehabilitation in patients with acute cerebral infarction by seculin. *Chin J Hosp Pharm* 2015;35:1768–71.
- [22] Neha , Sodhi RK, Jaggi AS, Singh N. Animal models of dementia and cognitive dysfunction. *Life Sci* 2014;109:73–86.
- [23] Zhang Y, Zhao H, Fang Y, et al. The association between lesion location, sex and post-stroke depression: meta-analysis. *Brain Behav* 2017;7:e00788.