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Investigation and analysis of cognitive function and psychological status in stroke patients with COVID-19

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Abstract **Objective** To investigate the clinical characteristics of COVID-19 patients with stroke and the changes of cognitive function and mental state within 6 months after discharge. **Methods** Retrospective analysis of 32 patients with COVID-19 complicated with stroke in the Third people's Hospital of Hubei Province from January 21 to June 1, 2020, and 32 patients with COVID-19 patients without stroke and 32 common pneumonia patients complicated with stroke treated in the same period as the control group. The clinical data and experimental parameters in the hospital were counted. They were followed up within 6 months after discharge, and the cognitive function of the patients was evaluated by Montreal cognitive function evaluation form, GAD-7 extensive anxiety scale and PHQ-9 depression scale, to test the psychological state of patients. The significant differences under three scores of the groups were analyzed, and the related risk factors of anxiety and depression were analyzed by binary logistic regression. **Results** Kruskal-wallisH test showed that there was a significant difference in cognitive score, anxiety score, depression score among groups($P<0.05$). Binary logistic regression analysis showed that female gender ($P = 0.004$) and COVID-19 infection($P < 0.001$) were independent risk factors for anxiety and depression in stroke population. **Conclusion** COVID-19 was indeed associated with prognosis anxiety and depression, but not with cognitive impairment. Women and patients with COVID-19 infection were independent factors of anxiety and depression in stroke population.

There are serious negative emotions such as anxiety and depression within 6 months after discharge, and there are still many psychological problems. After discharge, taking corresponding psychological intervention for patients can maintain their mental health and promote disease rehabilitation.

Key words: COVID-19; stroke; cognitive function; psychological status; clinical characteristics

1.Introduction

In January 7, 2020, New Coronavirus pneumonia was identified as New Coronavirus by virus typing [1]. In February 11, 2020, the WHO was named COVID-19. COVID-19 mainly acts on the respiratory system, but it can also invade the nervous system. This invasion of the nerve shows neurophilia [2]. Studies have shown that the incidence of acute cerebrovascular disease has increased the risk of death by 3 times in COVID-19 patients [3]. We can see that COVID-19 and stroke have an interaction with each other, and COVID-19 increases the incidence rate of stroke, meanwhile stroke also makes COVID-19 more risk of death.

The post-stroke cognitive impairment (PSCI) is considered as the most common complication after stroke.At present, the pathogenesis of PSCI has not been fully elucidated, and most studies believe that the mechanisms of cerebrovascular injury, brain neurodegeneration, inflammation, and oxygen free radical damage are related to the pathogenesis of PSCI[4-5]. Considering the COVID-19 also damages the neural function, and this impairment of the neural function may have some influence on the cognitive function. We hypothesis that COVID-19 patients combined with stoke may have more severe PSCI.

After stroke, it is easy to lead to post-stroke depression (PSD), and PSD will also aggravate the cognitive dysfunction of stroke patients, and then delay the rehabilitation process of patients after stroke[7].PSCI not the only has a serious impact on patients' ability of daily life,what's more, it can place a heavy burden on families and society; and PSCI may even develop into dementia with increasing age [8]. During the COVID-19 epidemic, COVID-19 patients also have a series of psychological stress reactions, among which depression and anxiety are the main psychological symptoms, leading to sympathetic and parasympathetic nervous system activation, producing somatic symptoms, and further aggravating or deteriorating the condition.

This study will focused on the clinical characteristics of COVID-19 patients with stroke, especially on the Montreal cognitive assessment scale (MoCA), PHQ-9 depression scale and GAD-7 extensive anxiety scale. Further more, we explore the cognitive function and psychological status changes of COVID-19 patients with stroke within 6 months after discharge.

2. Data and Methods

2.1 Case collection Refers to the diagnosis criteria of Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Trial Version 5, Revised Edition)[9].From January 1 to June 1, 2020, the paper and electronic medical records of inpatients were reviewed continuously in the Department of Neurology and surgery of the third people's Hospital of Hubei Province.After detailed evaluation of inclusion and exclusion criteria, 32 patients with COVID-19 complicated with stroke were included in this study. Inclusion criteria: (1) ischemic and hemorrhagic stroke was diagnosed according to the international classification of diseases (ICD-10), and the location of infarction and hemorrhage was confirmed by cerebral CT or MRI. (2) The infected patients were confirmed by RT-PCR detection of SARS COV-2 RNA. (3) The patient was admitted within 1

week after the onset of stroke. (4) Age ≥ 40 years old. The exclusion criteria : (1) previous diagnosis of anxiety, depression and other mental disorders. (2) Severe aphasia, confused thinking or unable to complete the relevant scale test. (3) There are other diseases that can cause mood disorders, including severe heart failure, thyroid disease and severe liver and kidney dysfunction.

2.2 Data collection The clinical symptoms and laboratory test results of all patients were collected and summarized through the standard case information form, and followed up to November 20, 2020. The follow-up time was within 6 months after discharge, and the follow-up was conducted by telephone [10]. The follow-up content was the scores of Montreal cognitive function evaluation form (MoCA), GAD-7 extensive anxiety scale and PHQ-9 depression scale.

2.3 Methods and Groups They were divided into non stroke with COVID-19 group, COVID-19 combined with stroke group and stroke combined with common pneumonia group, with 32 cases in each group. The symptoms, laboratory results, CT findings of lung and head at admission were recorded, and follow-up questionnaires were conducted for patients in each group. The follow-up date was November 20, 2020. The contents of the questionnaire were psychological function assessment (GAD-7 extensive anxiety scale and PHQ-9 Depression Scale) and cognitive function assessment (Montreal Cognitive Assessment scale).

2.4 Statistical Methods Spss23.0 was used for all statistical analysis. T-test or chi square test was used for the comparison between normal distribution measurement data groups, Kruskal wallish test was used for the comparison of multiple independent samples for nonparametric test, and binary logistic regression analysis was used for binary variables. The difference was statistically significant ($P < 0.05$).

3 Results

3.1 Clinical Data and Features A total of 32 COVID-19 patients complicated with stroke were diagnosed. The age range was 49-82 years old. There were 28 cases of ischemic stroke (88.24%) and 4 cases of hemorrhagic stroke (11.76%). Eighteen patients were male, accounting for 56.7% 18/32 . The initial and main clinical symptoms of the patients were headache (37.50%, 12 / 32), fever (43.75%, 14 / 32), limb weakness (31.25%, 10 / 32), cough (37.50%, 12 / 32) , as shown in Table 1. The proportion of lymphocytes in COVID-19 patients complicated with stroke (75.00%, 24 / 32)was lower than that of non stroke COVID-19 patients (84.38%, 27 / 32), but higher than that of common pneumonia patients complicated with stroke (50.00% , 16 / 32, $P < 0.05$) . Non stroke COVID-19 patients(84. 38%, 27 / 32) had a highest proportion of neutrophils in groups, while stroke patients with common pneumonia was the lowest (37. 50%, 12 / 32), and the difference was statistically significant ($P < 0.05$). Although there were differences in leukocyte, hemoglobin concentration, platelet, blood creatinine, C-reactive protein, blood potassium, blood sodium and procalcitonin among the groups, the difference was not statistically significant ($P > 0.05$, Table 2).

Table 1 Clinical characteristics analysis of 32 COVID-19 patients combined with stroke (n,%)

Clinical characteristics	Non-stroke COVID-19	COVID-19 with stroke	Common pneumonia combined with stroke COVID-19 negative	*P*
Stroke type				
Ischemic		28	30	>.99

hemorrhagic		4	2	
average age	68	65.9	72.1	
age				
40-60	10 31.25	12 37.50	6 18.75	.25
60-80	18 56.25	18 56.25	16 50.00	
>80	4 12.5	2 6.25	10 31.25	
sex				
male	17 53.13	18 56.25	22 68.75	.53
female	15 46.87	14 43.75	10 31.25	
symptom	9 28.13	10 31.25	8 25.00	.59
Headache,	1 3.13	0	2 6.25	
dizziness	16 50.00	14 43.75	18 56.25	
vomit	5 15.63	10 31.25	10 31.25	
fever	16 50.00	12 37.50	12 37.50	
weak				
cough				

Table 2 Early Laboratory Index of 32 COVID-19 Patients with Stroke (n,%)

metric	Non-stroke COVID-19	COVID-19 with stroke	Common pneumonia with stroke COVID-19 negative	*P*
Leukocyte	7.95	7.87	8.39	
cells (10 ^ 9 / L)	3.50-17.12	3.47—16.47	3.29—16.48	
(3.5-9.5)				
<3.5	3 9.38	2(6.25)	2 6.25	.85
3.5-	22 68.75	22(68.75)	22 68.75	
>9.5	7 21.87	8(25.00)	8 25.00	
Lymphocyte	12.96	13.89	21.69	
s (%)	2.50—35.00	3.40—22.40	8.30—46.30	
(20-50)				
<20	27 84.38	24(75.00)	16 50.00	<0.05
Neutrophils	85.63	79.46	70.01	
(%) (40-75)	58—90.50	65.90—89.80	47.20—88.30	
>75	27 84.38	22(68.75)	12 37.50	<0.05
Haemoglobin (g / l)	321	336.00	333.19	
	310.00—350.50	300.00—374.00	305.00—357.00	
(316-354)				
<316	3 9.38	2(6.25)	4 12.50	.73
Platelet (g / l),	225.38	211.75	243.27	
	110.00—310.00	102.00—325.	0.26—470.00	

(125-350)		00		
<125	5 15.63	6(18.75)	4 12.50	.45
ALT (U / L)	25.98	26.14	28.29	
(5-40)	5.00—39.75	10.00—52.50	10.00—48.70	
>40	3 9.38	4(12.50)	4 12.50	.62
AST (U / L)	38.21	42.33	32.03	
(8-40)	15.00—38.50	19.00—113.5 0	18.90—61.50	
>40	8 25.00	10(31.25)	6 18.75	.29
Urea	7.93	7.76	8.78	
nitrogen	3.12—10.59	2.66—22.90	2.32—52.01	
(mmol/L)				
(3-9.2)				
>9.2	6 18.75	6(18.75)	6 18.75	.82
creatinine	118.32	151.44	78.50	
(u mol/L)	40.00—150.00	41—1063	48.00—190.00	
(44-120)				
>120	5 15.63	8(25.00)	2 6.25	.32
Globulin (g	30.56	29.58	30.80	
/ L) (20-40)	15.65—39.75	18.00—40.00	19.6—40.7	
<20	2 6.25	2(6.25)	2 6.25	.52
A/G(1.2-2.4	1.31	1.28	1.24	
)	0.49—2.13	0.75—2.35	0.82—1.98	
<1.2	15 46.86	14(43.75)	16 50.00	.68
CRP(mg/L)	59.85	62.21	38.69	
(0-5)	1.00—246.72	1.00—276.82	1.00—131.47	
>5	20 62.50	22(68.75)	26(81.25)	.52
Na^+(mmol/	140.21	139.21	136.99	
L) (135-145)	132.00—149.10	133.00—151. 50	116.20—145.10	
<135	3 9.38	4(12.50)	6(18.75)	.32
K^+(mmol/L)	3.85	3.71	4.12	
(3.5-5.5)	2.98—5.19	2.82—5.20	3.20—6.11	
<3.5	11 34.38	14(43.75)	4 12.50	.86
PCT(ng/ml)	2.76	2.66	0.21	
(0.04-0.25)	0.06—35.72	0.04—22.19	0.04—0.49	
>0.25	12 37.50	10(31.25)	10 31.25	.54

3.2 The analysis of cognitive, anxiety and depression scores among the three groups To evaluated the differences in MOCA cognitive score, GAD-7 anxiety score and PHQ-9 depression score among non stroke COVID-19 patients, COVID-19 patients with stroke and common

pneumonia patients with stroke. The results of H-Test analysis showed that there were significant differences in three scores among three groups (P < 0.05), as shown in Table 3. Comparative analysis showed that there was a significant difference in cognitive score among non stroke COVID-19 patients, COVID-19 patients with stroke and common pneumonia patients with stroke. (P<0. 05). In terms of anxiety score and depression score, there also were a significant difference among the three groups (P<0. 05). As shown in Table 3, there was a significant difference in anxiety score and depression score between pneumonia combined with stroke and COVID-19 infection with stroke (P<0. 05). These results indicated that COVID-19 infection may aggravate the anxiety and depression of stroke patients.

Table 3 Analysis of cognitive, anxiety and depression scores among the three groups [Median (25%Q, 75%Q)]

	Moca Cognitive score	GAD-7 Anxiety Score	The PHQ-9 Depression Score
Non-stroke COVID-19	22 22 23	12 9 14	11 7 16
COVID-19 with stroke	15 11 18 *	12 11 14 #	11 8 16 #
Common pneumonia with stroke COVID-19 negative	13 8 17 &	2 1 5 &	5 2 8 &
P	<0.05	<0.05	<0.05

* means compared with the non stroke group (P < 0.05),& indicates compared with the non stroke group (P < 0.05), # indicating compared with the group of common pneumonia complicated with stroke (P < 0.05)

3.3Independent risk factors for anxiety, depression and cognitive function in COVID-19 patients combined with stroke Considering that there are significant differences in MOCA cognitive score, GAD-7 anxiety score and PHQ-9 depression score among non stroke COVID-19 patients, COVID-19 patients with stroke and common pneumonia patients with stroke, this part aim to explore risk factors for anxiety, depression and cognitive function in COVID-19 patients combined with stroke. The gender, stroke type, whether suffering from COVID-19 infection and age and so on were bringing into binary logistic regression as predictors. Multivariate analysis showed that female (P = 0.004), suffering from COVID-19 infection (P < 0.001) were independent risk factor for anxiety and depression in stroke population, as shown in table 4-5. There were not any risk factors for cognitive function in COVID-19 patients combined with stroke, as shown in table 6.

Table 4 Multivariate logistic regression analysis of anxiety-related factors in stroke patients

							95% C.I.for EXP(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Gender (1)	3.458	1.185	8.516	1	.004	31.767	3.113	324.152
Stroke type (1)	-.009	1.062	.000	1	.993	.991	.124	7.945

Whether COVID-19 (1)	5.316	1.441	13.608	1	.000	203.589	12.080	3431.012
Age (1)	-1.781	1.021	3.045	1	.081	.168	.023	1.245
Constant	-4.605	1.569	8.610	1	.003	.010		

Table 5 Multivariate logistic regression analysis of depression-related factors in stroke patients

							95% C.I.for EXP(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Gender (1)	2.315	.924	6.276	1	.012	10.124	1.655	61.929
Stroke type (1)	-.717	1.006	.508	1	.476	.488	.068	3.508
Whether COVID-19 (1)	2.811	1.175	5.720	1	.017	16.627	1.661	166.428
Age (1)	.769	.884	.757	1	.384	2.157	.382	12.198
Constant	-4.794	1.542	9.664	1	.002	.008		

Table 6 Multivariate logistic regression analysis of factors related with cognitive function in stroke patients

							95% C.I.for EXP(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Gender (1)	.190	.732	.067	1	.795	1.209	.288	5.081
Stroke type (1)	.429	.792	.294	1	.588	1.536	.325	7.256
Whether COVID-19 (1)	.223	.785	.081	1	.776	1.250	.268	5.821
age	-.707	.747	.896	1	.344	.493	.114	2.132
Constant	1.597	.708	5.089	1	.024	4.936		

4 Discussion

In this study, COVID-19 patients with stroke had early symptoms of fever, cough, headache and limb weakness. The type of stroke was mainly ischemic type (88.24%). In the laboratory test indicators, the lymphocyte count of most COVID-19 patients combined with stroke is reduced, suggesting that SARS-CoV-2 may act on lymphocytes, especially T lymphocytes. Like SARS-CoV, inhibiting the cellular immune function of the body, SARS-CoV-2 also may also could aggravate ischemic brain injury through triggering cytokine cascade reaction [11-12]. Critically ill patients with severe SARS-CoV-2 infection usually show elevated D-dimer levels and severe thrombocytopenia, making patients more prone to acute cerebrovascular events [13]. In this study, most patients have normal platelet values, and only 6 patients have mild platelet values, which may be related to the fact that the cases collected in this study are not severe, most of them were with mild SARS-CoV-2 infection.

This study explored the changes of cognitive score, anxiety score and depression score in COVID-19 patients with stroke. Through Kruskal wallish test, we found that patients with COVID-19 infection are indeed related to prognosis anxiety and depression, which will increase

the psychological burden. A study found that novel coronavirus pneumonia patients may have some type of cognitive impairment in the long term, especially in the areas of processing speed, verbal memory or executive function [14]. Our study found that novel coronavirus pneumonia is associated with stroke and cognitive impairment also in mild and non severe infection, but not only in severe infection.

Then through binary logistic regression, the data reveled that women and patients with COVID-19 infection were independent risk factors of anxiety and depression in stroke population, rather than of cognitive function. Previous study evaluating depression and anxiety symptoms also found that female patients were more likely to be anxious than male patients in stroke [15]. The results showed that even if COVID-19 patients with stroke have recovered, the disease will have a residual effect on the subsequent psychology of patients, causing anxiety and depression after discharge, which has a great negative impact on people's psychology and behavior. Specifically, the reason why patients have strong psychological changes in the follow-up may be that they do not know enough about their diseases. During hospitalization, both of the COVID-19 and stroke have brought strong psychological pressure to patients. The isolation during hospitalization makes patients have emotions such as fear, worry and confusion, and they often fell powerless and are at a loss, resulting in high anxiety and depression. This change in psychological status can even continue until a few months after the patientleaves the hospital. Fear of incomplete treatment and recurrence, or fear of increasing the burden on the family may be the reason for the persistence of anxiety and depression after recovery. Studies have shown that the physical and social functions of patients with depression are significantly reduced, and the disease recurrence rate and mortality of patients are increased, which seriously affects the neurological function and daily living ability of patients, and then increases the economic burden of families [7]. So, the public healthy system should pay attention to this part, and improve the scientific advocacy system about COVID-19.

Therefore, during the COVID-19 epidemic, under the double blow of COVID-19 infection and stroke, COVID-19 and stroke patients need more physiological and psychological treatment, and the treatment not only needs to provide patients in hospital. Attention should also be paid to the continuous state of psychological changes after discharge. Give comfort and care to discharged patients, dredge their bad emotions, implement timely psychological crisis intervention measures and help patients make scientific self-regulation, arouse patients' positive emotions and play the role of psychological defense, so as to improve and eliminate negative emotions such as depression [16], which plays a positive role in improving the prognosis of COVID-19 patients with stroke and reducing the disease recurrence rate and mortality [17].

This study has some limitations. First of all, the number of cases is not enough and there are few, which will lead to the deviation of the experimental results. Secondly, the follow-up is conducted in the form of telephone, so it is impossible to communicate with the patient face-to-face and judge the patient's look and mental state in real time, which may lead to the score being not comprehensive and accurate.

5.Conclusions

In conclusion, the follow-up of stroke patients with COVID-19 infection found they have more serious anxiety and depression, and this negative psychological state persists for a period of time after discharge, which hinders the recovery of neurological function and ability of daily living.

Female, suffering from COVID-19 infection were independent risk factor for anxiety and depression in stroke.

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