

The influence of COVID-19 on the treatment of patients with acute ischemic stroke: a retrospective observational study

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Abstract

Introduction: Since December 2019, coronavirus 2019 (COVID-19) has rapidly spread to become a global pandemic, exerting a great pressure on medical staff worldwide. This study aimed to observe whether COVID-19 influenced the diagnosis and treatment of ischemic stroke (IS).

Material and methods: This study retrospectively analysed the clinical data (number of emergencies, time from onset to treatment, and door-to-needle time [DNT]) of patients with acute IS (AIS) treated in our hospital within six months of the first case of COVID-19 reported in the city; the derived data were then compared with the situation of patients during the same period in 2019.

Results: The results showed that the number of medical visits during the period of COVID-19 decreased by 44.3%, and the median time from the onset of IS to emergency treatment was 35 min longer than that during the same period in 2019. The median time from entering the emergency department to the completion of cranial computerized tomography was 8 min shorter than during the same period in 2019, and the median time of DNT was relatively shorter than that during the same period in 2019.

Conclusions: The pandemic situation of COVID-19 significantly reduced the number of patients with AIS and prolonged the travel time to the hospital whereas most of the stroke treatment services were maintained.

Key words: ischemic stroke, COVID-19, DNT, medical behaviour, public health.

Introduction

Ischemic stroke (IS) is a destructive disease with high mortality and disability. Timely and effective reperfusion treatment for IS can significantly improve prognosis. At present, reperfusion therapy, which is also the most effective treatment for acute IS (AIS), is unanimously recommended by domestic and foreign guidelines [7,12]. It is known that reperfusion therapy is strictly limited by the treatment time window, and the time window of intravenous thrombolysis is 4.5 h. To save as many patients as possible within the time window, stroke centres actively promote the construction of green channels for stroke to optimize hospital procedures and shorten thrombolysis, or door-to-needle time (DNT) [4,9]. Whether the patient arrives at the hospital in time after the onset of the disease (the time from the onset to the hospital), and whether the DNT can be controlled at an ideal level after admission has become the main factor affecting reperfusion treatment for IS [16].

Whether to visit a doctor in time after the onset of the disease is often affected by many factors, such as the level of health knowledge of patients, the knowledge of correct first aid procedures for stroke and urban traffic [11]. Whether the patients are quickly identified and screened after admission, given timely auxiliary

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examinations, and whether can be treated guickly are the key factors controlling DNT [13,14]. Since the emergence of coronavirus 2019 (COVID-19) in December 2019, it has rapidly evolved into a global pandemic, exerting a great pressure on medical staff around the world [5]. China has implemented strict public health measures against COVID-19, strengthened medical resources for the screening of suspected patients, and implemented the isolation and treatment of infected patients [3]. For example, it may have affected the public's behaviour around seeking medical treatment, making people hesitant about going to the hospital and may delay their treatment [17,22]. It is uncertain whether the treatment services for AIS will be affected by the provision of stroke green channel treatment and the allocation of the labour force and medical resources, which may prolong the DNT because of the response to the pandemic situation [6,19]. Therefore, this study aimed to explore the impact of the pandemic on the attendance of patients with AIS, including the number of visits, time from onset to treatment, and DNT.

Material and methods

This paper retrospectively analysed the clinical data of selected patients with AIS to compare the arrival time (onset to hospital), computerized tomography (CT) completion time, and DNT of patients admitted and treated with the stroke green channel in the primary stroke centre of our hospital. Inclusion criteria included: 1) typical symptoms of AIS with confirmation by head CT and/or magnetic resonance imaging (MRI); 2) age \geq 18 years old; 3) admission to the hospital through the green channel of stroke; and 4) patients with stroke symptoms or when the patient was last known to be "normal" within 24 hours. Exclusion criteria included: 1) patients referred by other hospitals; 2) severe respiratory failure, heart failure, or acute coronary syndrome; and 3) coexisting confirmed or suspected COVID-19. We selected all patients meeting these criteria who had been admitted from 19 January to 18 July 2020 as the COVID-19 group, following the first confirmed case of COVID-19 in Beijing. Similar patients admitted from 19 January 2019 to 18 July 2019 were included in the control group. All patients diagnosed and suspected of having COVID-19 were transferred to designated hospitals under the guidelines of the National Health Commission; as such, they were excluded from this study. The diagnosis of IS was confirmed by the attending neurologist.

Baseline demographic statistics, past medical history, vascular risk factors, the National Institute of Health Stroke Scale, and details of acute stroke treatment were retrieved from the database of the Emergency Department of Beijing Shijingshan Hospital for the selected patients. The evaluation indicators included the number of medical visits, onset-to-door time, door-to-CT time, and the DNT. Onset-to-door time was defined as the time from the onset of symptoms to the emergency room. Door-to-CT time was defined as the time from arrival at the emergency room to the completion of the CT scan. The DNT was the time from arrival at the emergency room to intravenous injection of the recombinant tissue plasminogen activator. This study was approved by the research ethics committee of our hospital.

Statistical analysis

The SPSS Statistics 20.0 statistical software was used to analyse the data. The measurement data were expressed by an independent sample *t*-test, and the counting data were expressed as percentages and compared by a χ^2 test; p < 0.05 was a statistically significant cut-off value.

Results

From 19 January to 18 July 2020, 39 patients were admitted to the COVID-19 group after excluding three patients (two from other hospitals and one with coexisting severe respiratory failure). Meanwhile, 70 patients comprised the control group in the corresponding period in 2019 after seven patients were excluded (four from other hospitals and three with coexisting severe respiratory failure, heart failure, or acute coronary syndrome). The number of medical visits during the epidemic decreased by 44.3% compared with the same period in the previous year, indicating a significant difference. There were no significant differences in age, sex, body weight, or risk factors for previous cerebrovascular disease and stroke severity between the two groups (Table I). In the COVID-19 group, the time from the onset of IS to the emergency visit was relatively longer than in the control group (135 [104-171] vs. 100 [60-135] min, p = 0.013) (Table II). The time from entering the emergency department to the completion of cranial CT of the COVID-19 group was relatively shorter than that of the control group (12 [10-21] vs. 20 [14-25] min, p = 0.028). In the COVID-19 group, the DNT was relatively shorter than in the control group (38 [30-43] vs. 44 [32-60] min, *p* = 0.009) (Table II).

Discussion

During the pandemic period, the number of patients decreased significantly, and the time taken to see a doctor was significantly longer than in the corresponding period a year earlier. This situation was related to the reduction of public mobility during the pan-

	COVID-19 (<i>n</i> = 39)	Pre-COVID-19 (<i>n</i> = 70)	P-value
Male, n (%)	29 (74.4)	51 (72.9)	0.84
Age (years), mean ±SD	66 ±12.3	68.5 ±12.4	0.11
Weight (kg), mean ±SD	70.3 ±9.1	69.0 ±11.0	0.53
Diabetes mellitus, n (%)	12 (30.8)	17 (24.3)	0.46
Hypertension, n (%)	22 (56.4)	45 (64.3)	0.42
Hyperlipidemia, n (%)	10 (25.6)	16 (22.9)	0.74
Coronary heart disease, <i>n</i> (%)	11 (28.2)	23 (32.9)	0.62
Atrial fibrillation, n (%)	4 (10.2)	8 (11.4)	0.85
Cerebral infarction, n (%)	10 (25.6)	16 (22.8)	0.74
Blood sugar (mmol), mean ±SD	7.2 ±1.9	8.1 ±3.3	0.12
Median baseline NIHSS, median (IQR)	5 (2-8)	4 (3-9)	0.88

Table I. Demographic data and clinical characteristics of patients

demic period, which may have affected the willingness of patients to seek medical help for acute symptoms. The COVID-19 pandemic is widespread with strong infectivity and high early mortality, and medical workers and the media have been urging people to stay at home as much as possible. Because of media publicity and the strict implementation of public health control measures, this pandemic is reminiscent of infectious diseases such as severe acute respiratory syndrome. This has caused panic within the Chinese society [15] that patients who worry about going to the hospital in the pandemic context will increase their risk of infection with COVID-19 [10]. According to a previous largescale research survey, during the intensifying COVID-19 pandemic, 98.54% of the respondents said they were 'very scared' and 94.45% worried about themselves or their families being infected [8]. The stroke centre in New Jersey reported that the number of new stroke diagnoses decreased by an average of 38% during the pandemic [18]. Considering that the decrease in the number of patients and the delay in visiting doctors in this study were related to fear caused by the COVID-19 pandemic, where patients chose to wait at home for their symptoms or the pandemic situation to improve and were reluctant to go to the hospital, an optimal treatment time could easily have been missed. Patients should be encouraged to seek medical treatment through social media or other information sources, and

Table II. Diagnosis and treatment before and after entering the hospital

	COVID-19 (n = 39)	Pre-COVID-19 (<i>n</i> = 70)	P-value
Onset-to-door time (min), median (IQR)	135 (104-171)	100 (60-135)	0.013
Door to CT time (min), median (IQR)	12 (10-21)	20 (14-25)	0.028
Door-to-needle time (min), median (IQR)	38 (30-43)	44 (32-60)	0.009

hospitals should ensure to make every effort to prevent contact with potentially infectious patients.

Stroke is a destructive disease with high mortality and disability. However, in ordinary patients with no medical background of this condition, both personally and in their families, there is a lack of knowledge of stroke, making it easy to attribute their symptoms to other diseases or believe that the disease can be resolved through self-healing [21]. Therefore, in the pandemic context, it is recommended to raise and maintain public awareness of stroke, particularly about the importance of a timely diagnosis and treatment of acute neurological symptoms.

The time to complete the CT and DNT was relatively reduced after admission to the hospital. According to our statistical results, the time from admission to the completion of CT was significantly reduced, and the reduction of DNT was mainly because of the reduction of time to complete CT. We found that in the COVID-19 pandemic context, not only did the number of stroke patients decrease, but the overall number of people who went to the hospital decreased significantly. This proportion was far greater than the limited medical resources that hospitals could provide because of the pandemic. Compared with the corresponding period in the previous year, the time for patients to receive a doctor consultation, complete physical examination, and complete auxiliary examination was significantly shorter when patients went through the stroke green channel. This was consistent with our results. From another point of view, it also proves the importance of optimizing the in-hospital consultation process for shortening DNT [20]. The reason why the time from the completion of CT to intravenous thrombolysis was slightly longer during the study's COVID-19 period was because of the additional requirements for the prevention and control of nosocomial infection. In this way, the preparation time before obtaining informed consent and the puncture operation was increased.

The COVID-19 pandemic has significantly reduced the number of patients with AIS and prolonged the time of treatment, which has harmed the treatment of AIS. The reasons for this are mainly related to the psychological fear of patients and their families during brought on by COVID-19 and a lack of knowledge or attention to the treatment of stroke in the acute stage. The significant shortening of DNT in this period once again confirmed from different perspectives that reducing the waiting time can significantly shorten DNT when there is no significant improvement in the diagnosis and treatment level of medical staff and the allocation of medical resources. The results of this study suggest that, when dealing with major public health emergencies, public psychological counselling should be increased to help ease the fear of patients. In addition, public education on the general knowledge of infectious diseases should be strengthened through various channels, and public health knowledge of stroke, especially first aid for cerebrovascular diseases, should be improved, and the importance of immediate medical treatment should be emphasized. It is necessary to make patients and their families realize that stroke is a destructive disease with high mortality and disability rates and that delaying or not seeking treatment will adversely affect the prognosis of stroke. The timely and effective treatment of AIS, particularly the reperfusion treatment of IS, can significantly improve the prognosis and avoid delaying the best time for stroke treatment. Although our stroke centre recruited medical staff to assist in the fight against COVID-19, we reorganized the staff promptly so that most of the stroke treatment services were maintained. Every effort was made to ensure that AIS treatment was not affected. Stroke centres should actively optimize the in-hospital consultation process and make continuous improvements to further shorten the DNT because if the waiting time is too long it will harm the treatment of AIS.

The limitations of this study are its retrospective nature and that only a few patients managed in a single primary stroke centre in Beijing were included; therefore, future research is needed with multi-centre, multi-regional, and larger sample coverage. There are some factors, like the changes in patients' medical behaviours and the number of ambulances available during the COVID-19 period that may have affected the study results. Further study is needed to consider the affecting factors and their control within the methodology; for example, excluding patients with irregular medical behaviours. In addition, studies on stroke associated with COVID-19 pneumonia have been observational and retrospective, and no studies have assessed the risk of stroke after the onset of COVID-19 [1,2]. This study only analysed the impact of the pandemic on stroke patients and the hospital treatment process, and did not prove whether these changes impacted the prognosis of patients; further research is required to confirm this. This study was conducted during the early stages of COVID-19 pneumonia incidence in China and we do not know whether these findings have changed in the context of the current Omicron pandemic.

Conclusions

In conclusion, in the early stages of the novel Coronavirus pandemic, the number of visits for stroke patients declined significantly compared to the prepandemic stage. The time between onset of symptoms and hospital visit was significantly longer whereas the stroke treatment services were maintained, even with a relatively shorter time from the emergency room to intervention.

Data access statement

All relevant data are within the paper and its supporting information files.

Disclosure

The authors report no conflict of interest.

References

- 1. Arroja MM, Reid E, McCabe C. Therapeutic potential of the renin angiotensin system in ischaemic stroke. Exp Transl Stroke Med 2016; 8: 8.
- Divani AA, Andalib S, Di Napoli M, Lattanzi S, Hussain MS, Biller J, McCullough LD, Azarpazhooh MR, Seletska A, Mayer SA, Torbey M. Coronavirus disease 2019 and stroke: clinical manifestations and pathophysiological insights. J Stroke Cerebrovasc Dis 2020; 29: 104941.
- Du Q, Zhang D, Hu W, Li X, Xia Q, Wen T, Jia H. Nosocomial infection of COVID-19: A new challenge for healthcare professionals (Review). Int J Mol Med 2021; 47: 31.
- 4. Goyal N, Tsivgoulis G, Pandhi A, Malhotra K, Krishnan R, Ishfaq MF, Krishnaiah B, Nickele C, Inoa-Acosta V, Katsanos AH, Hoit D, Elijovich L, Alexandrov A, Arthur AS. Impact of pretreatment with intravenous thrombolysis on reperfusion status in acute strokes treated with mechanical thrombectomy. J Neurointerv Surg 2019; 11: 1073-1079.
- Handberry M, Bull-Otterson L, Dai M, Mann NC, Chaney E, Ratto J, Horiuchi K, Siza C, Kulkarni A, Gundlapalli AV, Boehmer TK. Changes in emergency medical services before and during the COVID-19 pandemic in the United States, January 2018-December 2020. Clin Infect Dis 2021; 73 (Suppl 1): S84-S91.
- Hoyer C, Ebert A, Huttner HB, Puetz V, Kallmünzer B, Barlinn K, Haverkamp C, Harloff A, Brich J, Platten M, Szabo K. Acute stroke in times of the COVID-19 pandemic: a multicenter study. Stroke 2020; 51: 2224-2227.
- 7. Lees KR, Emberson J, Blackwell L, Bluhmki E, Davis SM, Donnan GA, Grotta JC, Kaste M, von Kummer R, Lansberg MG, Lindley RI, Lyden P, Murray GD, Sandercock PA, Toni D, Toyoda K,

Wardlaw JM, Whiteley WN, Baigent C, Hacke W, Howard G; Stroke Thrombolysis Trialists' Collaborators Group. Effects of alteplase for acute stroke on the distribution of functional outcomes: a pooled analysis of 9 trials. Stroke 2016; 47: 2373-2379.

- Li C, Xu J, Yue L, Shen M, Dai M, Liu N. Knowledge, attitude, and practice survey regarding coronavirus disease 2019 among residents in Hunan Province. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2020; 45: 665-672.
- 9. Lou M, Ding J, Hu B, Zhang Y, Li H, Tan Z, Wan Y, Xu AD, Chinese Stroke Association Stroke Council Guideline Writing Committee. Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update on organizational stroke management. Stroke Vasc Neurol 2020; 5: 260-269.
- Markus HS, Brainin M. COVID-19 and stroke-A global World Stroke Organization perspective. Int J Stroke 2020; 15: 361-364.
- Mouthon-Reignier C, Bonnaud I, Gaudron M, Vannier-Bernard S, Bodin JF, Cottier JP, De Toffol B, Debiais S. Impact of a direct-admission stroke pathway on delays of admission, care, and rates of intravenous thrombolysis. Rev Neurol (Paris) 2016; 172: 756-760.
- 12. Neuroimmunology Branch of Chinese Society for Immunology, Department of Neuroimmunology of Chinese Medical Association Neurology Branch & Neuroimmunology Commissioner of Chinese Medical Doctor Association of Neurology. Chinese expert consensus on diagnosis and treatment of primary central nervous system vasculitis. Chin J Neuroimmunol Neurol 2017; 24: 229-239.
- 13. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, Zhang X, Pais P, Agapay S, Lopez-Jaramillo P, Damasceno A, Langhorne P, McQueen MJ, Rosengren A, Dehghan M, Hankey GJ, Dans AL, Elsayed A, Avezum A, Mondo C, Diener HC, Ryglewicz D, Czlonkowska A, Nana Pogosova A, Weimar C, Iqbal R, Diaz R, Yusoff K, Yusufali A, Oguz A, Wang X, Penaherrera E, Lanas F, Ogah OS, Ogunniyi A, Iversen HK, Malaga G, Rumboldt Z, Oveisgharan S, Hussain FA, Magazi D, Nilanont Y, Ferguson J, Pare G, Yusuf S, INTERSTROKE investigators. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet 2016; 388: 761-775.
- 14. Park PSW, Frost T, Tan S, Wong J, Pope A, Dewey HM, Choi PMC. The quest to reduce stroke treatment delays at a Melbourne metropolitan primary stroke centre over the last two decades. Intern Med J 2022; 52: 1978-1985.
- Rabaan AA, Al-Ahmed SH, Sah R, Al-Tawfiq JA, Al-Qaaneh AM, Al-Jamea LH, Woodman A, Al-Qahtani M, Haque S, Harapan H, Bonilla-Aldana DK, Kumar P, Dhama K, Rodriguez-Morales AJ. Recent advances in vaccine and immunotherapy for COVID-19. Hum Vaccin Immunother 2020; 16: 3011-3022.
- 16. Saber H, Khatibi K, Szeder V, Tateshima S, Colby GP, Nour M, Jahan R, Duckwiler G, Liebeskind DS, Saver JL. Reperfusion therapy frequency and outcomes in mild ischemic stroke in the United States. Stroke 2020; 51: 3241-3249.
- Shehata IM, Elhassan A, Jung JW, Urits I, Viswanath O, Kaye AD. Elective cardiac surgery during the COVID-19 pandemic: Proceed or postpone? Best Pract Res Clin Anaesthesiol 2020; 34: 643-650.
- Siegler JE, Heslin ME, Thau L, Smith A, Jovin TG. Falling stroke rates during COVID-19 pandemic at a comprehensive stroke center. J Stroke Cerebrovasc Dis 2020; 29: 104953.
- Teo KC, Leung WCY, Wong YK, Liu RKC, Chan AHY, Choi OMY, Kwok WM, Leung KK, Tse MY, Cheung RTF, Tsang AC, Lau KK.

Delays in stroke onset to hospital arrival time during COVID-19. Stroke 2020; 51: 2228-2231.

- 20. Tran D, Zhu Z, Shafie M, Abcede H, Stradling D, Yu W. Three easily-implementable changes reduce median door-to-needle time for intravenous thrombolysis by 23 minutes. BMC Neurol 2019; 19: 300.
- 21. Zhao B, Zhao YH, Jian WU. Analysis of the reasons for delayed admission of patients with acute ischemic stroke in beijing area. Chin Gen Pract 2015; 18: 684-687.
- 22. Zhao Z, Bai H, Duan J, Wang J. Recommendations of individualized medical treatment and common adverse events management for lung cancer patients during the outbreak of COVID-19 epidemic. Thorac Cancer 2020; 11: 1752-1757.