European Review for Medical and Pharmacological Sciences 2022; 26: 5574-5580

Impact of COVID-19 on acute ischemic stroke presentation and prognosis in a county-level stroke center

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Abstract. – OBJECTIVE: The COVID-19 pandemic has influenced regular medical procedures and health-seeking behaviors. In this study, we aimed to investigate the influence of the COVID-19 pandemic on the presentation and prognosis of acute ischemic stroke (AIS) patients in county-level stroke centers.

PATIENTS AND METHODS: We retrospectively collected AIS patients during the strict lockdown period (January 24, 2020, to March 27, 2020) and the corresponding "new normal" period (2021) of the COVID-19 pandemic. Patients seen during the same timeframe in 2019 were enrolled as controls. Statistical analysis was conducted to compare the clinical characteristics of AIS patients who presented during the lockdown and new normal periods and those who presented during the pre-COVID-19 pandemic period.

RESULTS: A total of 134 AIS patients presented during the lockdown period (the 2020 group), 207 patients in the pre-COVID-19 period (the 2019 group) and 201 patients in the "new normal" period (the 2021 group). Compared to the 2019 group, there was approximately 1/3 reduction in the number of patients who presented during the lockdown period, while the number of patients who received IVT or EVT was similar between the two groups. The number of patients, baseline characteristics, workflow intervals and clinical outcomes presented during the "new normal" period were similar between the 2019 and 2021 groups. Logistic regression showed that lockdown or new normal status were not risk factors associated with a poor outcome at 90 days.

CONCLUSIONS: In county-level city stroke centers, the COVID-19 lockdown resulted in a reduction in the number of patients with AIS admitted to the hospital but had no effect on patients treated with IVT or EVT. Lockdown or new normal status did not influence the prognosis of AIS patients.

Key Words:
COVID-19, Acute ischemic stroke, County-level, Stroke center.

Introduction

Since the outbreak of the COVID-19 pandemic, China has implemented several nation-wide strategies for preventing and containing the spread of the disease[1], such as social distancing, quarantine, pathogen testing, and other strategies[2,3], which simultaneously influence not only regular medical procedures but also health-seeking behaviors. The pandemic has also led to psychological distress and job burnout among medical staff[4,5], which has had an impact diagnosis and treatment activities. Studies from many countries have reported negative effects of the COVID-19 pandemic on the care of acute ischemic stroke (AIS) patients[6-15]; however, there are no reports on the impact of the pandemic on the diagnosis and treatment of AIS in county-level stroke centers in China. Chinese county hospitals provide primary neurological care services in most areas[16]. Some county hospitals have built stroke centers and are responsible for performing thrombectomies/thrombolysis for the AIS patients in the region[17]. Compared with the advanced stroke centers in municipal hospitals or teaching hospitals, these hospitals may have relatively weak medical skills[17], but their smaller radiation ranges may have advantages in prehospital emergency procedures[18]. Therefore, the currently reported impact of the COVID-19 pandemic on AIS treatment may not be applicable to the stroke centers in county hospitals.

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As a county-level stroke center, we developed this research to investigate the influence of the COVID-19 pandemic on the attendance and prognosis of AIS patients. We hope our findings will help treat AIS patients in county-level stroke centers during future malignant infectious disease pandemics.

Patients and Methods

Study Participants

All patients came from the stroke center of Jingjiang People's Hospital, which is the only medical unit in this county that performs intravenous thrombolysis (IVT) and endovascular treatment (EVT) and is responsible for the treatment of 800,000 people in the region. All AIS patients entered the green channel for stroke after visiting the emergency department. Like most advanced stroke centers in China, patients are given priority for diagnosis and treatment according to the principle of "diagnosis first and payment later". IVT is performed in the CT room or emergency room, and patients with indications for EVT bypass the ward and are sent to the DSA room.

At 24:00 on January 24, 2020, Jiangsu Province issued the first-level response to COVID-19 prevention and control and started the strictest control measures[19], such as maintaining social distance, limiting the flow of humans, stopping unnecessary business activities, and closing schools. These measures continued until 24:00 on March 27, 2020, and the pandemic prevention and control were adjusted to the three-level response[20]. In early April 2020, China successfully emerged from the first wave of the COVID-19 pandemic, and social activities gradually resumed[21]. After that, the control intensity has been gradually reduced, eventually to a "new normal", which consists of maintaining physical and social distancing, wearing a protective face mask, undergoing temperature checks, inquiring into people's recent travel history, writing down one's name and identification number and scanning a quick response code[22].

We collected AIS patients during the strict lockdown period (January 24, 2020, to March 27, 2020) and the corresponding "new normal" period (2021) of the COVID-19 pandemic from the prospectively registered stroke database of Jingjiang People's Hospital. Patients in the same period in 2019 were collected as controls.

Data Collection and Outcome Measures

We derived the data from the Green Channel of Stroke. The messages that were prospectively collected were as follows: age, sex, medical history, pretreatment National Institutes of Health Stroke Scale (NIHSS) score, vital signs, laboratory and neurovascular imaging results, workflow intervals, and clinical outcomes. The workflow intervals included the onset-to-door time (OTD), door-to-needle time (DNT), door-to-puncture time (DPT), and puncture-to-recanalization time (PRT). The short-term clinical outcome was defined as the modified Rankin scale (mRS) at 90 days, and patients with an mRS score of 0-2 were deemed to have a favorable outcome.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of Jingjiang People's Hospital and was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Because it was a retrospective study and did not include any personal information related to the participants, the need to obtain written informed consent was waived. The treatment of each participant during hospitalization was approved by the patient or their close family member, and a written informed consent form was obtained before treatment.

Statistical Analysis

SPSS 21.0 statistical software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. For normally distributed continuous variables (described as the mean±SD), analysis was performed using unpaired Student's *t*-tests. For nonnormally distributed continuous variables (described as the median [interquartile range (IQR)]), the Wilcoxon test was performed for analysis. Categorical variables (described as numbers (percentages)) were analyzed by the chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant. Binary logistic regression was conducted to identify the risk factors associated with poor outcome at 90 days in AIS patients during the lockdown period and "new normal" period.

Results

A total of 134 AIS patients presented during the lockdown period (the 2020 group), in comparison to 207 patients in the pre-COVID-19 peri-

Table I. Baseline and clinical characteristics of the three groups.

	2019 (n=207)	2020 (n=134)	2021 (n=201)	*p*1 (2019-2020)	*p*2 (2019-2021)
Age/year	69 (61-77)	73 (62-79)	70 (59.5-77)	0.072	0.848
Male	124 (59.9)	78 (58.2)	119 (59.2)	0.822	0.920
Smoking	76 (36.7)	51 (38.1)	60 (29.9)	0.819	0.172
Drinking	79 (38.2)	49 (36.6)	63 (31.3)	0.819	0.177
Hypertension	159 (76.8)	103 (76.9)	150 (74.6)	1.000	0.645
Diabetes	71 (34.3)	36 (26.9)	72 (35.8)	0.154	0.757
Hyperlipidemia	4 (1.9)	4 (3.0)	10 (5.0)	0.717	0.108
AF	9 (4.3)	11 (8.2)	15 (7.5)	0.160	0.210
CAD	21 (10.1)	18 (13.4)	22 (10.9)	0.386	0.872
Stroke classification				0.013	0.240
Large atherosclerotic stroke	100 (48.3)	62 (46.3)	95 (47.3)		
Cardiogenic cerebral embolism	43 (20.8)	47 (35.1)	50 (24.9)		
Arteriolar occlusive stroke	59 (28.5)	23 (17.2)	50 (24.9)		
Other or unknown etiology	5 (2.4)	2 (1.5)	6 (3.0)		
IVT	20 (9.7)	20 (14.9)	19 (9.5)	0.168	1.000
EVT	16 (7.7)	15 (11.2)	16 (8.0)	0.335	1.000
OTD	115 (60-170)	102.5 (68.8-166.3)	101 (66.5-167.5)	0.768	0.654
DNT	41.5 (33.3-51.0)	39.5 (32.5-45.5)	36 (30-42)	0.635	0.086
DPT	88 (85-90)	80 (76-85)	89.5 (81.3-92)	0.005	0.733
PRT	50.5 (48-63)	55 (51-61)	58.5 (49.3-74)	0.191	0.157
Baseline NIHSS	3 (2-7)	8.5 (6-13)	3 (2-6)	<0.001	0.320
3m-mRS	1 (0-3)	3 (1-4)	1 (0-3)	<0.001	0.880
3m-mRS 0-2	149 (72.0)	58 (43.3)	146 (72.6)	<0.001	0.912

AF, atrial fibrillation; CAD, coronary heart disease; IVT, intravenous thrombolysis; EVT, endovascular treatment; OTD, onset-to-door time; DNT, door-to-needle time; DPT, door-to-puncture time; PRT, puncture-to-recanalization time; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale.
*p*1: the lockdown period in 2020 compared to the corresponding period in 2019; *p*2: the "new normal" period in 2021 compared to the corresponding period in 2019.

od (the 2019 group) and 201 patients in the "new normal" period (the 2021 group).

Baseline Characteristics, Time Metrics and Outcomes in the 2019 and 2020 Groups

Compared to the 2019 group, there was an approximately 1/3 reduction in the number of patients who presented during the lockdown period, while the number of patients who received IVT or EVT was similar between the two groups. The 2020 group had a higher proportion of patients with cardiogenic cerebral embolism stroke and a lower proportion of patients with arteriolar occlusive stroke. The median time of DPT in the 2020 group was 80 (76-85) min, which was significantly less than that in the 2019 group (88 (85-90) min, p=0.005). The median admission NIHSS score in the 2020 group was 8.5 (6-13), which was significantly higher than that in the 2019 group [(3 (2-7), p<0.001)]. The 2020 group had a worse clinical outcome, with a median 3m-mRS of 3 (1-4), which was significantly higher than that in the 2019 group, with a median 3m-mRS of 1 (0-3), p<0.001. A total of 72.0% of patients in the 2019 group had favorable outcomes, while only 43.3% of patients in the 2020 group had favorable outcomes (p<0.001) (Table I). The distribution of the mRS scores at 3 months for AIS patients is shown in Figure 1.

Binary logistic regression showed that the baseline NIHSS was an independent risk factor associated with poor outcome at 90 days in AIS patients in the non-COVID-19 pandemic and the lockdown period and that the "lockdown" was not an independent risk factor (Table II).

Baseline Characteristics, Time Metrics and Outcomes in the 2019 and 2021 Groups

The number of patients who presented during the "new normal" period was similar to the 2019 group, and the baseline characteristics, workflow intervals and clinical outcomes were also similar between the two groups (Table I, Figure 1). Binary logistic regression showed that older age, CAD, and baseline NIHSS were independent risk factors associated with poor outcome at 90 days

Table II. Risk factors associated with poor outcome at 90 days in patients with acute ischemic stroke in the non-COVID-19 pandemic and the lockdown periods.

	Favorable outcome (n=207)	Poor outcome (n=134)	Unadjusted OR	p	Adjusted OR	p
Lockdown	58 (28)	76 (56.7)	3.366 (2.132-5.316)	0.000	1.489 (0.849-2.613)	0.165
Female	115 (55.6)	87 (64.9)	0.675 (0.431-1.057)	0.086	0.535 (0.255-1.121)	0.097
Age	69 (62-77)	73 (61.5-79)	1.012 (0.994-1.031)	0.202	1.006 (0.983-1.029)	0.614
Smoking	69 (33.3)	58 (43.3)	1.526 (0.976-2.388)	0.064	1.209 (0.594-2.460)	0.602
Drinking	73 (35.3)	55 (41)	1.278 (0.817-1.998)	0.282	0.827 (0.409-1.670)	0.596
Hypertension	166 (80.2)	96 (71.6)	0.624 (0.375-1.037)	0.069	0.578 (0.315-1.063)	0.078
Diabetes	69 (33.3)	38 (28.4)	0.792 (0.493-1.272)	0.334	0.871 (0.488-1.556)	0.641
Hyperlipidemia	5 (2.4)	3 (2.2)	0.925 (0.217-3.937)	0.916	0.369 (0.052-2.611)	0.318
AF	12 (5.8)	8 (6)	1.032 (0.410-2.595)	0.947	0.991 (0.331-2.970)	0.987
CAD	27 (13)	12 (9)	0.656 (0.320-1.344)	0.249	0.576 (0.242-1.373)	0.214
IVT	18 (7.2)	22 (13.4)	2.062 (1.060-4.012)	0.033	1.306 (0.550-3.100)	0.545
EVT	16 (7.7)	15 (11.2)	1.505 (0.717-3.156)	0.280	0.862 (0.318-2.334)	0.770
Baseline NIHSS	4 (2-7)	9.5 (6-15)	1.275 (1.202-1.353)	<0.001	1.260 (1.179-1.347)	<0.001

AF, atrial fibrillation; CAD, coronary heart disease; IVT, intravenous thrombolysis; EVT, endovascular treatment; NIHSS, National Institutes of Health Stroke Scale.

in AIS patients in the non-COVID-19 pandemic, and the "new normal" was not an independent risk factor (Table III).

Discussion

In this study, we found that during the lockdown period of the COVID-19 pandemic, the number of patients admitted to our stroke center had decreased. According to the baseline NIHSS scores, we found that some AIS patients with mild symptoms did not visit doctors. However, patients who received IVT or EVT were not influenced during the lockdown period. Meanwhile, during the "new normal" period, the number of patients who underwent IVT or EVT and were admitted to the hospital and the workflow intervals were also not influenced.

Infection prevention and control (IPC) is the most effective way to break the transmission chain of the virus[23-25]. However, IPC may influence the AIS workflow[25,26]. Studies in the international literature have generally reported a decline in hospital admissions during the COVID-19 period compared with the pre-COVID-19 period. For example, Kristoffersen et al[27] found a 29.91% decrease in Norway, Butt et al[28] found a 12.66% decrease in Denmark, Sacco et al[29] found a 24.36% decrease in Italy, and Tan et al[30] found a 36.42% (63/173) decrease in Chongqing, China. Our study first reported data showing a 35.3% decrease in a county-level stroke center.

The median admission NIHSS in the 2020 group was 8.5, which was significantly higher than that in the 2019 group. Combined with the reduction in the total number of patients with AIS, we identified there were fewer patients with mild symptoms who were admitted to the stroke center for treatment. We speculate that the possible reasons are as follows: (1) during the strict lockdown period, patients with mild stroke were not able to attract enough attention from the control and screening staff in order for the patient to seek medical treatment[31]; (2) patients refused to seek medical treatment for fear of COVID-19 infection[32]. Like us, most county-level cities in China have only one hospital that has a stroke center responsible for treating the entire county-level city's population[17]. During the strict lockdown period, the primary hospitals were closed. Therefore, these patients with AIS who did not seek medical treatment had no other effective treatment, and they did not receive risk factor assessment and reasonable secondary prevention guidance. Therefore, we believe that the strict blockade period of IPC should focus on the treatment of mild stroke and build a reasonable process to effectively screen and treat stroke patients.

Although the total number of patients with AIS decreased, the number of patients who underwent IVT or EVT did not decrease. During the COVID-19 pandemic period, patients in our center underwent epidemiological investigations to exclude high-risk COVID-19 patients and to undergo nucleic acid testing before entering the

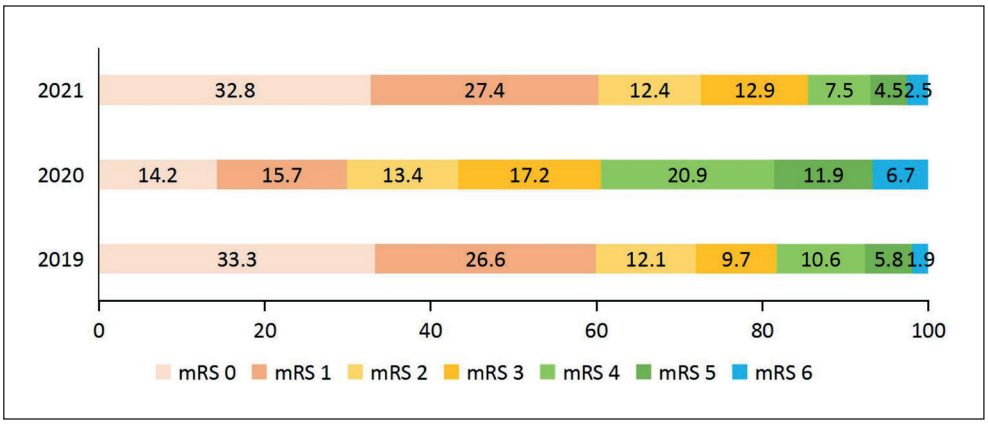

Figure 1. MRS at 3 months in the three groups of AIS patients. mRS, modified Rankin Scale; AIS, acute ischemic stroke.

ward or DSA room. Because all emergency patients can be admitted to a single room before the nucleic acid results are available, even those at high risk of COVID-19 do not lose access to IVT or EVT, which may be the reason why the number of patients who underwent IVT or EVT did not decrease. Unlike our study, Xu et al[15] observed that the COVID-19 lockdown led to a reduction in patients with IVT. Their stroke center is a prefecture-level stroke center, and patients may have more choices. During the COVID-19 pandemic period, patients may be transferred to other nearby hospitals for treatment. However, the overall medical technology in county-level cities is relatively weak. As the only stroke center that performs IVT/EVT, there is no possible transfer site for patients who need IVT/EVT treatment, and severe symptoms in patients can attract the attention of control and screening staff.

Our study found that in county-level stroke centers, the DNT of patients with IVT was not prolonged, and the DPT of patients with EVT was even 8 minutes less than usual, which is consistent with the study by Tan et al[30]. This may be due to fewer acute stroke patients coming to the hospital, freeing up more medical labor and reducing the waiting time for patients to use medical devices. A well-established green stroke channel guarantees the prognosis of hospitalized AIS patients. Although the median 3m-mRS score of patients in the lockdown period was 3 points, which was higher than 1 point before the COVID-19

Table III. Risk factors associated with poor outcome at 90 days in patients with acute ischemic stroke in the non-COVID-19 pandemic and "new normal" periods.

	Favorable outcome (n=295)	Poor outcome (n=113)	Unadjusted OR	*p*	Adjusted OR	*p*
New normal	146 (49.5)	55 (48.7)	0.968 (0.627-1.493)	0.882	1.129 (0.668-1.907)	0.651
Female	173 (58.6)	70 (61.9)	0.871 (0.558-1.359)	0.543	0.683 (0.333-1.401)	0.298
Age	68 (60-76)	74 (65-79)	1.038 (1.018-1.059)	0.000	1.043 (1.018-1.069)	0.001
Smoking	95 (32.2)	41 (36.3)	1.199 (0.761-1.889)	0.434	1.164 (0.582-2.329)	0.668
Drinking	103 (34.9)	39 (34.5)	0.982 (0.623-1.55)	0.939	0.736 (0.367-1.476)	0.388
Hypertension	228 (77.3)	81 (71.7)	0.744 (0.455-1.216)	0.238	0.701 (0.385-1.276)	0.245
Diabetes	106 (35.9)	37 (32.7)	0.868 (0.548-1.374)	0.546	0.999 (0.57-1.748)	0.996
Hyperlipidemia	13 (4.4)	1 (0.9)	0.194 (0.025-1.498)	0.116	0.525 (0.063-4.372)	0.551
AF	16 (5.4)	8 (7.1)	1.329 (0.552-3.196)	0.526	0.641 (0.194-2.112)	0.465
CAD	35 (11.9)	8 (7.1)	0.566 (0.254-1.261)	0.164	0.337 (0.124-0.917)	0.033
IVT	18 (6.1)	21 (18.6)	3.513 (1.793-6.88)	0.000	1.367 (0.554-3.376)	0.498
EVT	17 (5.8)	15 (13.3)	2.503 (1.204-5.202)	0.014	1.522 (0.569-4.074)	0.403
Baseline NIHSS	3 (1-5)	7 (4-13.5)	1.297 (1.219-1.379)	0.000	1.278 (1.198-1.363)	0.000

AF, atrial fibrillation; CAD, coronary heart disease; IVT, intravenous thrombolysis; EVT, endovascular treatment; NIHSS, National Institutes of Health Stroke Scale.

pandemic period, the binary logistic regression showed that the admission NIHSS score was an independent risk factor for poor prognosis, and lockdown was not.

Under the "new normal" period after COVID-19 control, there was no difference in the number of AIS patients attending stroke centers compared to that before the COVID-19 pandemic, there was no difference in the number and proportion of IVT/EVT, and there was no difference in workflow intervals such as DNT and DPT, confirming that during the "new normal" period, although all patients still need to conduct epidemiological investigations and do nucleic acid testing before entering the ward or DSA room, this measure did not lead to a delay in the green channel process. Therefore, it is clear that the "new normal" prevention and control of COVID-19 in China did not affect the diagnosis and treatment of AIS in county-level stroke centers.

There are some limitations in our study. First, although the data were collected prospectively, as a single-center retrospective study, whether this data can be applied to other county-level stroke centers requires further research. In addition, there were only a dozen COVID-19 patients in this county-level city and considering the impact on the public medical resources in the presence of a large number of COVID-19 patients, this conclusion may not be generalized to a situation with a large number of COVID-19 patients.

Conclusions

In conclusion, in county-level city stroke centers, the strict lockdown during COVID-19 resulted in a reduction in the number of patients with AIS admitted to the hospital but had no effect on patients treated with IVT or EVT. The lockdown or new normal status did not influence the prognosis of AIS patients. During the strict lockdown period, special attention should have been given to the treatment of mild stroke. It is necessary to establish a reasonable process to screen patients with mild stroke and to carry out effective treatment.

Authors' Contributions

Yunlong Ding, Yan Liu, Yu Zang, Tingting Zhai, and Wenjuan Wang conceived and designed the study. All authors assessed and diagnosed the patients. All authors were involved in the acquisition, analysis and interpretation of the data with Yunlong Ding taking the primary role in statistical analysis. Yan Liu, Tingting Zhai, Wenjuan Wang, Yanrong Zhang, Can Wei, Lu Zhu, and Zhiqun Gu drafted the manuscript. All authors were involved in revising the manuscript critically and gave final approval of the manuscript.

Conflict of Interest

The authors have no conflict of interest to declare.

Acknowledgments

This work was supported by the Taizhou Municipal Science and Technology Bureau (CN) (SSF20200086) and the Fifth "311 Project" in Taizhou (RCPY202004).

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