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Watershed infarction in COVID-19: The necessity of neuroimaging in patients with subtle neurological symptoms

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Keywords
COVID-19; Stroke; Brain; Magnetic Resonance Imaging; Clinical Characteristics; White Matter; Cerebrovascular Disorders

Abstract

Background: Cerebrovascular diseases comprise a significant portion of neurological disorders related to coronavirus disease 2019 (COVID-19). We evaluated the clinical and imaging characteristics of a cohort of COVID-19 patients with stroke and also identified patients with watershed infarcts.

Methods: In this cross-sectional study, seventy-three COVID-19 patients with ischemic stroke were included between October 2020 and January 2021. Patients were evaluated based on the following clinical and imaging features: severity of COVID-19 (critical/non-critical), stroke type, presence/absence of clinical suspicion of stroke, medical risk factors, Fazekas scale, atherothrombosis, small vessel disease, cardiac pathology, other causes, and dissection (ASCOD) criteria classification, and presence or absence of watershed infarction. Clinical outcomes were assessed based on Modified Rankin Scale (MRS) and mortality.

Results: Most cases of ischemic stroke were due to undetermined etiology (52.1%) and cardioembolism (32.9%). In terms of imaging pattern, 17 (23.0%) patients had watershed infarction. Watershed infarction was associated with the clinically non-suspicious category [odds ratio (OR) = 4.67, P = 0.007] and death after discharge (OR = 7.1, P = 0.003).

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Patients with watershed infarction had a higher odds of having high Fazekas score (OR = 5.17, P = 0.007) which was also shown by the logistic regression model (adjusted OR = 6.87, P = 0.030). Thirty-one (42%) patients were clinically non-suspected for ischemic stroke. Critical COVID-19 was more common among patients with watershed infarct and clinically non-suspicious patients (P = 0.020 and P = 0.005, respectively). Patients with chronic kidney disease (CKD) were more prone to having stroke with watershed pattern (P = 0.020).

Conclusion: Watershed infarct is one of the most common patterns of ischemic stroke in patients with COVID-19, for which clinicians should maintain a high index of suspicion in patients with critical COVID-19 without obvious clinical symptoms of stroke.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a tremendous impact on global health and may generate long-term sequelae in survivors.[1] By July 2022, more than 565 million confirmed cases have been reported worldwide and more than 6.3 million people have died.[2] Although COVID-19 can present a wide range of clinical manifestations, neurological symptoms have been highlighted in numerous previous articles.[3,4]

Neurological findings in the context of COVID-19 include cerebrovascular disease (e.g., ischemic and hemorrhagic stroke), leukoencephalopathy, acute demyelinating disorders, cranial nerve problems, and even polyneuropathies.[5,6] The pathophysiology of COVID-19 may be partially explained by the SARS-CoV-2 surface protein spike binding to the human angiotensin-converting enzyme 2 (ACE2), which generates a pro-inflammatory environment, causing endothelial apoptosis and potential cellular damage beyond the endothelium. The exaggerated release of cytokines in combination with a prothrombotic state may explicate the high prevalence of complications such as venous and arterial thromboembolism.[7-9] Nevertheless, a specific causative mechanism of COVID-19 and stroke has not been completely elucidated.[10]

Few studies evaluated watershed infarction in patients with COVID-19.[11,12] No explicit agreement has been established on the frequency of watershed infarction in COVID-19-related stroke, mainly due to the discrepancies in imaging indications and management (e.g., patients with subtle neurologic symptoms typically do not undergo brain imaging worldwide).[8,9,13] This study aimed to evaluate the clinical and imaging characteristics of a cohort of COVID-19 patients with stroke and also identify patients with watershed infarcts.

Materials and Methods

Study design: This single-center, cross-sectional, and observational study included 73 adult patients admitted to the largest medical center exclusively designated for the care of patients with COVID-19 in the central part of Iran who had neuroimaging and clinical findings of stroke. The study period was between October 2020 and January 2021, during the country's third peak of the COVID-19 outbreak. This Health Insurance Portability and Accountability Act (HIPAA)-compliant study was approved by the Institutional Review Board of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.MED.REC.1400.300). Verbal consent to participate in this study was obtained from all patients, or their surrogates, by one of the co-investigators. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used for the preparation and writing of this manuscript.[14]

Subjects: All subjects tested positive for SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) had respiratory symptoms, viral pneumonia findings on chest computed tomography (CT), and neurologic (focal or non-focal) symptoms. Patients were admitted with concomitant COVID-19 infection and stroke-related symptoms or developed neurologic symptoms during the hospitalization stay. All patients underwent brain CT and/or magnetic resonance imaging (MRI). Diagnosis of stroke and its subtypes was made based on clinical and neuroimaging findings, in consensus by two neurologists F.K. (more than 15 years of experience) and M.S. (with more than 20 years of experience and neuroimaging fellowship).

We divided the cohort into two categories depending on the COVID-19 clinical severity (critical/non-critical). Critical cases were defined as "patients with respiratory failure, multiple organ dysfunction, and septic shock", as per the National Institute of Health (NIH) COVID-19 Treatment Guidelines.[15] Similarly, we evaluated our cohort based on the presence or absence of overt clinical suspicion of acute stroke (i.e., patients with focal neurological symptoms).[8] Patients without clinical suspicion of stroke and positive imaging findings of

stroke were labeled as "non-suspicious".

Data acquisition and variables: Demographic and clinical data were acquired from the patients directly or the patients' relatives upon enrollment. We collected medical risk factors for stroke: hypertension (HTN), diabetes mellitus (DM), ischemic heart disease (IHD), hyperlipidemia (HLP), heart failure (HF), atrial fibrillation (AF), chronic kidney disease (CKD), and malignancy. We also recorded admission vital signs and laboratory findings, duration of hospitalization, NIH Stroke Scale (NIHSS) (among patients with clinically suspected stroke), the time interval between the first COVID-19 symptoms and stroke diagnosis, and the number of deaths. An attending neurologist performed medical anamnesis and physical exams and categorized the patients as having clinical suspicion or non-suspicion of stroke.

According to imaging characteristics (brain CT/MRI), patients were categorized into the watershed and non-watershed infarction. The etiology of ischemic stroke was further evaluated with vascular imaging modalities and cardiac evaluations [including echocardiography and electrocardiogram (ECG)]. At least one of the standard vascular imaging modalities [cervical and transcranial color Doppler ultrasound, CT angiography, and magnetic resonance (MR) angiography] was performed for all patients except: 1) patients who left the hospital before completion of standard evaluation and 2) patients that their medical condition was not stable enough to transfer to radiology center.

Imaging characteristics, including stroke pattern, laterality, and vascular territory, were evaluated for all patients with ischemic stroke. Fazekas classification for lesions in the deep white matter (0 = absent, 1 = punctate foci, 2 = beginning confluence, 3 = large confluent areas) was assessed on axial fluid-attenuated inversion recovery (FLAIR) images.[16] Ischemic stroke subtypes were categorized according to ASCOD criteria classification as (A) atherothrombosis, (S) small-vessel disease, (C) cardiac pathology, (O) other determined causes, and (D) dissection.[17] Another category was defined to include patients with ischemic stroke with undetermined etiology that was later divided into two subcategories: undetermined etiology with negative results after standard evaluation (NSE) and undetermined etiology with incomplete standard evaluation (ISE). ISE subcategory was subdivided into three groups: patients who left the hospital against medical advice, patients who died without an established etiologic diagnosis, and patients without sufficient neurological evaluation. Patients were followed-up after three months with the Modified Rankin Scale (MRS) to evaluate the functional outcomes and sequel.[18] Regarding mortality, patients were categorized into two groups: death during hospitalization or death within three months after discharge.

Statistical analyses were conducted using SPSS software (version 21, IBM Corporation, Armonk, NY, USA). Quantitative results were presented as mean ± standard deviation (SD). Categorical variables were reported as frequency and percentage. Chi-square test was used to compare categorical variables and odds ratios (ORs) were calculated for two dichotomous variables. Independent t-tests and one-way analysis of variance (ANOVA) were applied to compare continuous variables between two and more than two groups, respectively. Binary logistic regression was performed to evaluate the effects of sex, clinical severity, CKD, duration between first COVID-19 symptoms and stroke diagnosis, presence of clinical suspicion of stroke, and having a high Fazekas score (score of 3) on the likelihood that patients had a watershed infarction.

Results

Patient's characteristics: Over the study period, seventy-three patients (37 women, 36 men) with a mean age of 71.50 ± 12.63 years fulfilled the eligibility criteria and were included in the study. The mean interval between the first symptoms of COVID-19 and stroke presentation was 13.05 ± 8.12 days. Ischemic stroke was suspected clinically in 42 patients and the mean NIHSS was 13.07 ± 7.00 among them. A total of 38 patients met the criteria for critical COVID-19, and 42 patients were admitted to the intensive care unit (ICU). Forty-four (60%) patients who had ischemic stroke died. The total number of deaths during hospitalization was 34 versus the ten deaths within three months after discharge. The mean MRS at the 3-month follow-up of patients with ischemic stroke was 4.63 ± 1.93. Table 1 summarizes the demographics, medical history, and hospitalization-related data of our cohort.

Type of stroke: According to the ASCOD classification, 32.9% of patients had cardioembolic stroke (n = 23), 2.7% other determined etiology (n = 2), 4.1% atherothrombosis (n = 3), 4.1% dissection (n = 3) and 2.7% small vessel disease (n = 2).

Table 1. Baseline characteristics of patients with coronavirus disease 2019 (COVID-19) and stroke

Variable			Value
Age (year)	Ischemic stroke (n = 73)		71.50 ± 12.63
Sex	Men		36
	Women		37
ASCOD category	Atherothrombosis		5 (6.8)
	Small vessel disease		2 (2.7)
	Cardiac pathology (cardioembolism)		23 (32.9)
	Other determined		2 (2.7)
	Dissection		3 (4.1)
	Other undetermined	All	38 (52.1)
		ISUE (NSE)	24
		ISUE (ISE)	14
Imaging characteristics	Laterality	Unilateral	50
		Bilateral	23
	Fazekas scale	0	9
		1	11
		2	17
		3	20
Duration between first COVID-19 symptoms and diagnosis of stroke (day)			13.05 ± 8.12
Ischemic stroke suspected clinically (n = 73)	Yes		42
	No		31
NIHSS in clinically suspected patients (n = 42)			13.07 ± 7.00
Hemodynamic status in admission	SBP (mmHg)		134.50 ± 31.40
	DBP (mmHg)		79.01 ± 19.60
	O_2 saturation		83.40 ± 7.70
Critical COVID			38
Admission in ICU			42
Duration of hospitalization (day)			15.58 ± 18.26
Length of ICU stay (day)			11.63 ± 8.55
PTE			7
Risk factors/comorbidities	HTN		49
	DM		42
	IHD		27
	HLP		13
	AF		18
	CKD		16
	Hypothyroidism		7
	Malignancy (liver, lymphoma, lung, brain, colorectal)		4
Outcome	Mortality	After 3 months	44 (60.2)
		In hospital	34
		After discharge	10
	MRS after 3 months		4.63 ± 1.93
		0	3
		1	4
		2	7
		3	7
		4	5
		5	3
		6	44

Data are presented as mean ± standard deviation (SD), number and percentage, or number

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ISUE: Ischemic stroke with undetermined etiology; NSE: Negative standard evaluation; ISE: Incomplete standard evaluation; COVID-19: Coronavirus disease 2019; NIHSS: National Institutes of Health Stroke Scale; ICU: Intensive care unit; PTE: Pulmonary thromboembolism; HTN: Hypertension; DM: Diabetes mellitus; IHD: Ischemic heart disease; HLP: Hyperlipidemia; AF: Atrial fibrillation; CKD: Chronic kidney disease; MRS: Modified Rankin Scale; ASCOD: Atherothrombosis, small vessel disease, cardiac pathology, other causes, and dissection

Patients whose etiology was other determined causes included one patient with reversible cerebral vasoconstriction syndrome (RCVS) and one with a hypercoagulable state due to

malignancy. A total of 38 (52.1%) patients had an undetermined etiology, including ISE (n = 14) and NSE (n = 24). Among the group with undetermined etiology and ISE, two patients requested to be discharged against medical advice, and 12 patients were critically ill/passed away within hours of admission (Table 1).

Imaging findings: All patients had brain MRI and/or CT. Fifty-seven patients had both MRI and CT, whereas 16 had CT only. In patients with ischemic stroke, 50 had unilateral cerebral hemisphere involvement, and 23 had bilateral involvement. Deep white matter hyperintense lesions were evaluated using the Fazekas scale in all patients with ischemic stroke who had an available brain MRI (n = 57) and were classified as absent (n = 9), punctate foci (n = 11), beginning confluence (n = 17), and large confluent areas (n = 20) (Table 1).

Clinical/imaging characteristics in patients with/without watershed infarction: Patients with watershed infarction had a longer interval time between the onset of COVID-19 symptoms and stroke occurrence (16.64 ± 7.38 vs. 11.52 ± 8.02, P = 0.02) and were associated with a higher incidence of critical COVID-19 cases (76% vs. 47%, P = 0.020). Among the comorbidities, only CKD was significantly more prevalent in subjects with watershed infarction [OR = 3.65, 95% confidence interval (CI): 1.10-12.14, P = 0.020]. Patients without clinical suspicion of stroke had higher odds (OR = 4.67, 95% CI: 1.43-15.22, P = 0.007) of having watershed infarction. Moreover, watershed infarction was highly associated with death within three months of discharge (OR = 7.1, 95% CI: 1.70-29.40, P = 0.003), whereas patients with stroke without watershed infarction had relatively higher odds of mortality during hospitalization (OR = 3.85, 95% CI: 1.09-12.99, P = 0.030). Moreover, watershed infarction was associated with a lower NIHSS among patients with clinically suspected stroke (5.25 ± 1.70 vs. 13.97 ± 6.81, P = 0.016). Regarding lesions seen on brain CT and/or MRI, bilateral hemispheric involvement was higher in the group with watershed infarction (OR = 6.72, 95% CI: 2.06-21.90, P = 0.001). Similarly, a high Fazekas score (i.e., 3) was associated with the development of acute watershed infarction (OR = 5.17, 95% CI: 1.49-17.81, P = 0.007). Among 17 patients with imaging patterns of watershed infarction, three patients had cardioembolic mechanism (AF rhythm), two patients had internal carotid artery stenosis (more than 70%), and others (n = 12) had no specific mechanism for ischemic stroke after preliminary evaluations. Details of all comparisons between patients with/without watershed infarction are presented in table 2 and figures 1 and 2.

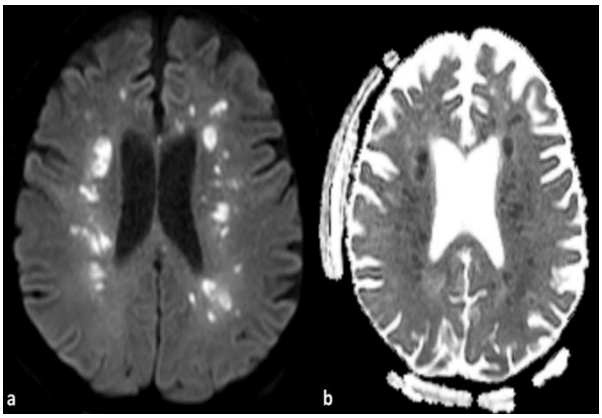

Figure 1. Deep acute watershed infarction. Brain magnetic resonance imaging (MRI) in a middle-aged woman with coronavirus disease 2019 (COVID-19) demonstrates ischemic stroke with bilateral watershed infarction in the axial diffusion-weighted imaging (DWI) (a) and apparent diffusion coefficient (ADC) map (b).

The logistic regression model was statistically significant (χ^2 = 17.55, P = 0.007). The model explained 44.4% (Nagelkerke pseudo R^2) of the variance in determining watershed infarction and correctly classified 84.4% of patients. Patients with high Fazekas score (i.e., 3) were 6.87 (95% CI: 1.14-41.28, P = 0.030) times more likely to have watershed infarction after adjusting relevant predictors.

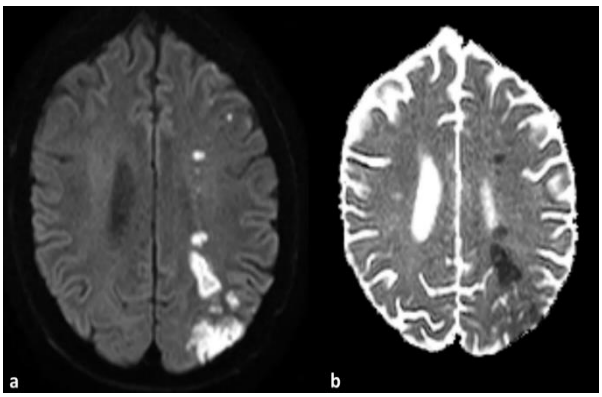

Figure 2. Deep and cortical acute watershed infarction. Brain magnetic resonance imaging (MRI) in a middle-aged man with coronavirus disease 2019 (COVID-19) shows a unilateral watershed territory infarct in the left middle cerebral/posterior cerebral arteries and the deep watershed territories as evident in the axial diffusion-weighted image (DWI) (a) and apparent diffusion coefficient (ADC) map (b).

Table 2. Comparison of clinical characteristics of ischemic stroke between patients with and without watershed infarction

Variable			Watershed infarction (n = 17)	Without watershed infarction (n = 56)	P
Age (year)			70.76 ± 11.19	71.73 ± 13.12	0.780
Sex	Men		8	28	0.830
	Women		9	28	
Duration between first COVID-19 symptoms and diagnosis of stroke (day)			16.64 ± 7.38	11.52 ± 8.02	0.020
Stroke suspected clinically			5	37	0.007
NIHSS in clinically suspected patients			5.25 ± 1.70	13.97 ± 6.81	0.016
SBP (mmHg)			128.06 ± 28.02	136.56 ± 32.36	0.340
DBP (mmHg)			70.00 ± 14.61	81.84 ± 20.24	0.030
O_2 saturation			83.51 ± 8.10	82.94 ± 6.40	0.790
Critical COVID			13	25	0.020
Admission in ICU			9	33	0.660
Duration of hospitalization (day)			19.52 ± 30.72	14.39 ± 12.47	0.310
Length of ICU stay (day)			11.22 ± 9.23	11.74 ± 8.51	0.870
PTE			0	7	0.120
HTN			11	38	0.810
DM			12	30	0.210
IHD			8	19	0.190
HLP			2	11	0.440
AF			3	15	0.440
CKD			7	9	0.020
Death	Total		10	34	0.890
	In hospital		4	30	0.030
	After discharge (3 months)		6	4	0.003
MRS after 3 months			4.76 ± 1.71	4.59 ± 2.00	0.740
Bilateral hemisphere involvement			11	12	0.001
Fazekas	0		1	8	0.050
	1		2	9	
	2		3	14	
	3		10	10	
ASCOD classification	Atherothrombosis		2	3	0.334
	Small vessel disease		0	2	
	Cardiac pathology		3	20	
	Other determined causes		0	2	
	Dissection		0	3	
	Other undetermined	ISUE (NSE)	12	12	
		ISUE (ISE)	0	14	

Data are presented as mean ± standard deviation (SD) or number

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ISUE: Ischemic stroke with undetermined etiology; NSE: Negative standard evaluation; ISE: Incomplete standard evaluation; COVID-19: Coronavirus disease 2019; NIHSS: National Institutes of Health Stroke Scale; ICU: Intensive care unit; PTE: Pulmonary thromboembolism; HTN: Hypertension; DM: Diabetes mellitus; IHD: Ischemic heart disease; HLP: Hyperlipidemia; AF: Atrial fibrillation; CKD: Chronic kidney disease; MRS: Modified Rankin Scale; ASCOD: Atherothrombosis, small vessel disease, cardiac pathology, other causes, and dissection

Clinical/imaging characteristics in patients with/without clinical suspicion of stroke: Patients without clinical suspicion of stroke had a longer time between the onset of COVID-19 symptoms and stroke occurrence (15.92 ± 9.62 vs. 10.27 ± 5.14, P = 0.007) and were associated with a higher incidence of critical COVID-19 cases (70.9% vs. 38.1%, OR = 3.97, 95% CI: 1.47-10.74, P = 0.005). In addition, patients without clinical suspicion of stroke had lower systolic blood pressure (SBP) (124.5 ± 22.3 vs. 142.1 ± 35.2, P = 0.02), diastolic blood pressure (DBP) (72.7 ± 17.4 vs. 83.8 ± 20.1, P = 0.020) and oxygen saturation (80.8 ± 8.4 vs. 85.3 ± 6.7, P = 0.010) in admission. In terms of neuroimaging, bilateral hemisphere involvement was more prevalent in patients without clinical suspicion of stroke (OR = 3.02, 95% CI: 1.09-8.39, P = 0.030). Details of comparisons between patients with and without clinical suspicion of stroke are shown in table 3.

Table 3. Comparison of clinical characteristics of ischemic stroke between patients with and without clinical suspicion of ischemic stroke

Variable		Stroke suspected clinically		P
		Yes (n = 42)	No (n = 31)	
Age (year)		71.61 ± 13.70	71.35 ± 11.24	0.930
Sex	Men	24	12	0.110
	Women	18	9	
Duration between first COVID-19 symptoms and diagnosis of stroke (day)		10.27 ± 5.14	15.92 ± 9.62	0.007
SBP (mmHg)		142.18 ± 35.23	124.51 ± 22.38	0.020
DBP (mmHg)		83.78 ± 20.10	72.75 ± 17.37	0.020
O_2 saturation		85.30 ± 6.68	80.77 ± 8.44	0.010
Critical COVID		16	22	0.005
Admission in ICU		21	21	0.130
Duration of hospitalization (day)		14.35 ± 13.38	17.25 ± 23.46	0.500
Length of ICU stay (day)		13.78 ± 9.67	9.28 ± 6.58	0.080
PTE		3	4	0.410
HTN		25	24	0.100
DM		23	19	0.570
IHD		14	13	0.780
HLP		6	7	0.320
AF		10	8	0.840
CKD		6	10	0.060
Death	Total	24	20	0.520
	In hospital	20	14	0.830
	After discharge (3 months)	4	6	0.230
MRS after 3 months		4.50 ± 2.01	4.80 ± 1.83	0.500
Bilateral hemisphere involvement		9	14	0.030

Data are presented as mean ± standard deviation (SD) or number

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; COVID-19: Coronavirus disease 2019; ICU: Intensive care unit; PTE: Pulmonary thromboembolism; HTN: Hypertension; DM: Diabetes mellitus; IHD: Ischemic heart disease; HLP: Hyperlipidemia; AF: Atrial fibrillation; CKD: Chronic kidney disease; MRS: Modified Rankin Scale

Discussion

The overall objective of this study was to determine the clinical and imaging findings of adult patients with COVID-19 and cerebrovascular accidents (CVAs) and to assess watershed infarcts in these patients. Most cases of ischemic stroke were due to undetermined etiology and cardiac pathology (i.e., cardioembolism).

The largest subgroup of our patients had undetermined stroke etiology, which is consistent with other reports.[19] Recent study performed before the onset of COVID-19 in Isfahan[20] reported 23.3% cardioembolic stroke, 13.9% large-artery atherosclerosis, 26.6% small vessel occlusion, 10.3% ischemic stroke of undetermined etiology and NSE, and 21.5% ischemic stroke of undetermined etiology and ISE. Reasons for differences between subtypes of stroke in our patients with COVID-19 and previous studies before COVID-19 pandemic are as follows: 1) high percentage of critically ill patients with unstable status and patients' death before completion of stroke workup, 2) because of patients' fear of being hospitalized in COVID center, 2 patients left the hospital with personal consent before any stroke workup, 3) slight manifestations of small vessel acute ischemic stroke (AIS) and patients' fear of going to COVID center could be stated as a reason for unexpected low percentage of small vessel AIS, and 4) most cases with watershed infarction (12/17) did not have any etiology, which could be related to short-term heart monitoring and incomplete vessel study. Apart from the expected etiology of ischemic stroke that impairs blood flow in large vessels, some authors have described a pattern of watershed white matter hyperintensities in patients with COVID-19,[11,12] which has also been found in this study in a large proportion. Sawlani et al. found that watershed white matter hyperintensities occurred in 20% of patients with COVID-19 with neurological manifestations, mainly in the deep white matter, the corpus callosum, and the cerebellar white matter.[11] Similarly, Katz et al. postulated that patients with severe COVID-19 had

a higher prevalence of multivascular territory infarction, including a watershed pattern and hemorrhagic transformation.[12]

In our study, we found that patients with a medical history of CKD were more prone to stroke with watershed patterns. Patients with CKD had a higher chance of having white matter disease, silent infarcts, and brain atrophy compared to the normal population.[21] This group of patients may experience hypotension or hemodynamic instability episodes, which makes them prone to perfusion-related brain injury.[22]

The Fazekas scale has been widely used to score the level of injury in the cerebral white matter and also predict outcomes in patients with cerebrovascular disease, such as functionality, stroke recurrence, and mortality.[23] In our cohort, patients with watershed infarction had a higher Fazekas scale in evaluating the deep white matter. We hypothesize that patients with chronic small vessel disease are more prone to having a watershed infarction. This may be related to the preexisting microvascular changes in this group of patients. Therefore, early neuroimaging is needed in these patients, even if they present with subtle neurological symptoms.

Of note, most of our patients with critical COVID-19 were not clinically suspected of stroke. This could be due to the excessive attention of clinicians to stabilizing the patient in respiratory and cardiovascular aspects, potentially overlooking the involvement of the central nervous system (CNS). The severity of the patient's cardiorespiratory status may also mask subtle neurologic symptomatology. For these reasons, special attention needs to be paid to patients with COVID-19 and risk factors for severity. Even if symptoms are not typical for stroke clinically, in addition to a meticulous neurologic examination, neuroimaging should be contemplated to rule out cerebrovascular events.

Our study found that in-hospital death was more frequent among patients without watershed infarct. However, death after discharge was more frequent in patients with watershed infarct. This difference may be explained by higher NIHSS among patients without watershed infarct, which resulted in higher in-hospital mortality. On the other hand, higher mortality of patients with watershed infarction within three months of discharge can be due to post-COVID complications and the severity of COVID-19.[24,25]

Limitations: We acknowledge that this study has some limitations that need to be addressed in future studies. First, since patients could have been asymptomatic or have mild symptoms, we anticipate the possibility of inaccuracy or recall bias regarding the exact moment of onset of COVID-19 symptoms and/or presentation of stroke. Second, 22% of our patients with ischemic stroke did not undergo brain MRI; therefore, Fazekas scoring could not be done for this group of patients.

Conclusion

Watershed infarction is a considerable part of patients with ischemic stroke, which should be considered in patients with critical COVID-19, patients without obvious clinical symptoms of stroke, and patients with chronic cerebral small vessel disease. Early neuroimaging in these patients could potentially expedite management and improve outcomes. Furthermore, special additional attention should be paid during the subacute and chronic stroke periods since fatalities tend to occur in high proportions after discharge in patients with watershed infarction.

Conflict of Interests

The authors declare no conflict of interest in this study.

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None.

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