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Evaluation of ischemic stroke patients associated with COVID-19

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ABSTRACT

Aims: Many neurological symptoms and complications, including stroke, may develop during Coronavirus disease-2019 (COVID-19). This study evaluated the risk, timing, prognosis, relationship between stroke and COVID-19, and treatment modalities of stroke due to COVID-19 by examining stroke patients with COVID-19.

Methods: This retrospective cross-sectional study included 12 patients aged ≥18 years with acute ischemic stroke and who were hospitalized with a confirmed diagnosis of COVID-19. In this study, demographic findings, clinical and stroke symptoms, stroke time, comorbid conditions that could pose a risk for stroke, inflammatory markers, D-dimer levels, imaging results, cardiologic evaluations, O_2 need, administered treatments, intensive care support, and prognosis were recorded retrospectively from patient files.

Results: Of the patients, 50% were male and 50% were female. The mean age was 70.6±9.3 (range, 55-84) years. The most common comorbid conditions were hypertension (58.3%) and diabetes mellitus (41.7%). Stroke developed at a median of 10.5 [interquartile range (IQR), 5-19.5] days after symptoms COVID-19. The mean National Institutes of Health Stroke Scale score was 7.8±4.7 (range, 3-18) (1-25). The average D-dimer and IL-6 levels of the patients were measured as 3.7 (IQR, 2.7-7.6) mg/L and 44.1±41.2 (range, 4.0-117) pg/mL, respectively. Most patients (66.7%) required oxygen during their hospitalization.

Conclusions: Patients with a stroke due to COVID-19 infection have several risk factors, particularly diabetes mellitus and hypertension. They had increased D-dimer levels, and most patients had severe disease. These results suggested that COVID-19 triggered or facilitated stroke rather than being an independent cause.

Introduction

On December 31st, 2019, the China Country Office for the World Health Organization (WHO) reported pneumonia cases with an unknown etiology in Wuhan, China. On January 7th, 2020, the agent was defined as a novel coronavirus that was not previously detected in humans (2019-nCoV). Later, the disease was named Coronavirus disease-2019 (COVID-19). Then, the WHO declared a pandemic on March 11th, 2020, upon detecting COVID-19 cases in 113 countries, excluding China and considering the spread and impact of the disease. COVID-19 causes many neurologic symptoms and signs, including stroke additional to the respiratory symptoms. Although the incidence of stroke is not known, the incidence was 0.9% in a study conducted in New York in patients with positive Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) tests (1-4). COVID-19 has a poor course in the elderly and those with hypertension, diabetes mellitus, heart disease, and obesity (5,6). Studies have reported an increased prevalence of neurological disorders in those with a severe COVID-19 infection. In a study conducted on 214 patients in Wuhan, although the overall incidence of stroke was 2.3%, it was 5.7% in patients with severe disease (7).

Several potential mechanisms have been identified for how COVID-19 increases the risk of stroke. These mechanisms are hypercoagulability evidenced by increased levels of D-dimer, cytokine storms indicative of excessive systemic inflammation or severe disease, and cardioembolism resulting from

virus-associated cardiac injury (8-10). The proinflammatory mechanisms during COVID-19 infection lead to increased clotting and disruption in vasomotor activity, which increases the risk for stroke (11). Further, recent studies have reported that COVID-19 acts on angiotensin-converting enzyme functional receptors, which have been implicated in severe cerebrovascular events, including stroke, among patients with risk factors for cerebrovascular diseases (CVD) (e.g., smoking or diabetes mellitus) (12-15). Despite the plethora of studies associating ischemic stroke with COVID-19, it has not yet been fully elucidated whether SARS-CoV-2 has a causal relationship with ischemic stroke.

This study evaluated the risk, timing, prognosis, relationship between stroke and COVID-19, and treatment modalities for stroke due to COVID-19 by examining stroke patients with COVID-19.

Methods

Study design and participants

In this retrospective cross-sectional study, the study population was patients with COVID-19 aged ≥18 years. This work was conducted at the University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Ankara, Türkiye. Medical records of the patients admitted to the COVID-19 clinic from September 2020 to January 2021 were evaluated. Of the patients, twelve with acute ischemic stroke and COVID-19 confirmed by laboratory tests (positive real-time reverse transcription-polymerase chain reaction results via nasopharyngeal swab) were included in the study. Patients with hemorrhagic stroke, cerebral venous thrombosis, negative COVID-19 test, suspected but not an imaging-confirmed acute stroke, and patients under 18 years of age were excluded.

COVID-19 infection was categorized according to the WHO classification (16). Mild COVID-19 was defined as respiratory symptoms without evidence of pneumonia or hypoxia, and moderate or severe infection was defined as the presence of clinical and radiological evidence of pneumonia. In moderate cases, SpO_2 ≥90% in room air, and one of the following was required to define severe disease: respiratory rate >30 breaths/min or SpO_2 <90% in room air (16). The severity of acute respiratory tract infection was defined according to oxygen demand and chest computed tomography (CT) scans. Low-flow oxygen therapy was defined as 1-6 $L.min^{-1}$ through a nasal cannula to keep a SpO_2 level of 90-92% (17). If the oxygen requirement was >6 L/min, it was accepted as a high oxygen demand. Body temperature ≥37.4 °C was considered fever. The stroke classification was based on the Trial of Org 1010172 in Acute Stroke Treatment (TOAST) classification (18).

The presence of new neurological symptoms that were confirmed by neuroimaging results was considered to be recurrent stroke.

Data collection

The study variables included demographic characteristics, COVID-19-related clinical and neurological symptoms, stroke time after the onset of COVID-19 symptoms, comorbid conditions associated with a higher risk of stroke [hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease (CAD), heart failure (HF), atrial fibrillation (AF), CVD, malignancy, and other conditions], inflammatory markers on admission [leucocyte, lymphocyte, neutrophil, C-reactive protein (CRP), procalcitonin, interleukin-6 (IL-6)]; D-dimer level closest to the stroke time, imaging findings [brain CT/CT angiography (CTA) and/or color Doppler ultrasonography (CDUS) and/or digital subtraction angiography (DSA) and magnetic resonance imaging (MRI) and chest CT] and cardiologic evaluations (transthoracic echocardiography and electrocardiography results); O_2 requirement, treatment, intensive care support, and prognosis (19,20).

Ethics

The study was approved by the Turkish Republic Ministry of Health (protocol no: 2021-03-27T11-00-17) and the University of Health Sciences Türkiye, Medical Ethics Committee (date: 17.06.2021, no: 2021-273). This study was conducted in accordance with the principles of the revised Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Version. 22.0 software (IBM Corp., Armonk, NY: USA). The normality of distribution was tested with Shapiro-Wilk for numerical data. In the descriptive analyses, frequencies, and percentages were used for categorical variables, and mean±standard deviation and median [interquartile range (IQR)] values were used for continuous variables according to the distribution.

Results

Demographic characteristics and clinical presentation

Of the 12 patients, 50% were female. The mean age was 70.6±9.3 years (range, 55-84 years) (Table 1). Eight (66.7%) patients were admitted with stroke, and four (33.3%) patients had a stroke during hospitalization. One patient had previous hospitalization due to COVID-19, and his disease was severe. Except for one (8.3%), 91.7% of the patients developed at least one symptom of COVID-19, such as fever, cough, shortness of breath, and gastrointestinal symptoms (Table 2).

Stroke occurred on average 10.5 (IQR, 5-19.5) days after symptoms of COVID-19 and as the first sign of COVID-19 in one patient. All patients had neurological findings due to posterior and/or anterior system involvement (Table 3). The mean stroke

severity was 7.8±4.7 points (range, 3-18) according to the National Institutes of Health Stroke Scale (1-25) score, with variability among patients (Table 3).

Laboratory findings

Except for one (8.3%) patient, 91.7% of patients had varying degrees of involvement on chest CT (Table 2). Among the inflammatory markers, mean CRP was 85.3±84.6 mg/L [(range: 0.6-236) (reference: 0-5 mg/L)] and IL-6 was 44.1±41.2 pg/mL [(range: 4.0-117) (reference: 0-5 pg/mL)]. Mean lymphocyte count was 1.1±0.70x10^3 cells/uL [(range: 0.4-2.7) (reference: 1.3-3.4x10^3 cells/μL.)] (Table 2). The median D-dimer level was 3.7 mg/L [(IQR 2.7-7.6) (reference: 0-0.5 mg/L)] and was high in all patients except two (Table 2).

Imaging

All patients had varying degrees of involvement in the posterior and/or anterior system on brain MRI and/or CT due to acute ischemic stroke (Table 3). We observed a large vessel occlusion (LVO) in 33.3% of the patients (Table 3). A hemorrhagic transformation developed in the infarct area of patient #2. Patient #12 had a subdural hematoma on the opposite side of the infarct area (Table 3).

Risk factors for stroke

Hypertension (58.3%), diabetes mellitus (41.7%), CAD (33.3%), AF (16.7%), prior CVD (16.7%), HF (25%), and malignancy (8.3%) were the most common risk factors for stroke (Table 1, 3).

Etiology of stroke

Two patients (16.7%) had a postulated cause of cardiogenic cause of stroke, AF. According to the TOAST classification, stroke due to large vessel atherosclerosis was present in 33.3%, cardioembolic stroke in 16.7%, lacunar stroke in 8.3%, and undetermined stroke in 41.7% of the patients (Table 3).

Clinical course and treatment

Most patients (66.7%) required oxygen during their hospitalization, and 75% had a high need for oxygen. Seven (58.3%) patients required intensive care during hospitalization. Steroid therapy was admistered to six (50%) patients, and one (8.3%) patient received immune plasma therapy. Low-molecular-weight heparin (LMWH) was not administered in the first stroke of patient #5 because this patient had a diagnosis of myelodysplastic syndrome (MDS), and the simultaneous platelet count was 9000. After the stroke recurred, LMWH treatment was administered considering the platelet count. All other patients received LMWH or intravenous heparin therapy (Table 2).

Thrombectomy was performed in one patient due to the presence of a thrombus formation protruding into the lumen in the middle part of the right common carotid artery (CCA), which impacted the wall in DSA (Table 3). On follow-up angiography, the part protruding into the lumen disappeared, and some thrombi impacted the wall persisted. Right CCA was found to be normal in CDUS performed at the follow-up 3 months later (Table 3).

One-quarter of the patients died (Table 3).

Patients with recurrent stroke

Stroke recurred in two (16.7%) patients 30 days after the first stroke in patient #5, and 24 days in patient #10 (Table 4). Among these patients, patient #5 had a high oxygen requirement during hospitalization (Table 2). D-dimer levels increased in both patients during their first and recurrent strokes. In the brain imaging of both patients, newly developed multiple infarct areas were detected in their recurrent strokes (Table 4). Both patients had underlying risk factors such as malignancy and CVD

Table 1. Baseline patient characteristics (n=12)

Age, years Mean±SD (min-max)	70.6±9.3 (55-84)
Female	n=6 (50%)
Hypertension	(n=7, 58.3%) (#1, 2, 6, 7, 9, 11, 12)
Diabetes mellitus	(n=5, 41.7%) (#1, 4, 7, 8, 11)
Atrial fibrillation	(n=2, 16.7%) (#3, 12)
Coronary artery disease	(n=4, 33.3%) (#2, 7, 11, 12)
Cerebrovascular disease	(n=2, 16.7%) (#5, 7)
Heart failure	(n=3, 25%) (#7, 11, 12)
Myelodysplastic syndrome	(n=1, 8.3%) (#5)
Malignancy	(n=1, 8.3%) (#10)
COPD	(n=2, 16.7%) (#2, 4)
Epilepsy	(n=1, 8.3%) (#11)

COPD: Chronic obstructive pulmonary disease, min-max: Minimum-maximum, SD: Standard deviation, #: Patients number

Table 2. COVID-19 related symptoms, inflammatory markers, D-dimer level, chest CT findings, O_2 requirement, intensive care support, and COVID-19 treatments (n=12)

Patient no.	Symptoms of COVID-19	Leukocytes (4.49-10.9x10^3 cells/µL*)	Neutrophil (2.1-8.89 x10^3 cells/µL*)	Lymphocyte (1.26-3.35 x10^3 cells/µL*)	CRP (0-5 mg/L*)	IL-6 (0-5 pg/mL*)	Procalcitonin (0-0.65 ng/mL*)	D-dimer (0-0.5 mg/L*)	Chest CT results	O_2 requirement	Intensive care support	Treatments of COVID-19
1	-	8.5	6	1.3	10.2	-	0.05	0.35	Bilateral multi-lober GGO	-	-	Steroid, LMWH
2	Cough, dyspnea, diarrhea	7.8	7.2	0.4	142	117	0.13	13.5	Bilateral multi-lober GGO	+, high	+	Steroid, LMWH
3	Anorexia, nausea	5.5	3.1	1.6	13.8	9.26	0.12	2.62	Bilateral peri-pheral multi-lober GGO	+	+	LMWH
4	Fever, cough	13.1	10.4	1.7	13	-	0.09	5.65	Bilateral peri-pheral lower lobes multi-focal GGO	+	+	IVH
5	Fever, dyspnea	2.6	1.9	0.4	236	36	3.23	4.28	Right upper lobe, multi-focal GGO	+, high	-	LMWH treatment according to the platelet count
6	Cough	5.6	2.3	2.7	0.6	3.97	-	0.46	N	-	-	LMWH
7	Cough, dyspnea	6	4.8	0.5	108	28	0.2	3.95	Bilateral patchy multi-lober GGO	+, high	+	Steroid, immune plasma, LMWH
8	Fever, dyspnea, cough	13.2	11.3	1.1	230	57.3	1.49	8.29	Bilateral multi-lober GGO	+, high	+	Steroid, LMWH
9	Cough	7.7	6.4	0.9	22.8	14.2	0.12	3.3	Peri-pheral bilateral GGO	-	-	LMWH
10	Cough	7.3	4.8	1.3	96	-	-	9.9	Right sub-pleural GGO	-	-	LMWH
11	Fever, cough	9.4	8.1	0,8	120	105	0.21	2.76	Bilateral multilober GGO	+, high	+	Steroid, LMWH
12	Dyspnea, cough, hemoptysis	14.1	12.2	0.8	31	26	-	3.54	Bilateral multilober GGO and paraseptal emphysematous changes	+, high	+	Steroid, LMWH

*Reference range.
CRP: C-reactive protein, IL-6: Interleukin-6, IVH: Intravenous heparinization, GGO: Ground-glass opacity, LMWH: Low-molecular-weight heparin, COVID-19: Coronavirus disease-2019, CT: Computed tomography

Table 3. Demographic features, acute ischemic stroke features, cardiac investigations, and clinical outcomes (n=12)

Patient no.	Age, sex	Risk factors for ischemic stroke	Clinical symptoms of ischemic stroke	NIHSS score	CT-MRI Stroke location	DSA -CTA- CDFI	ECG, ECHO	Stroke classification	Treatment for ischemic stroke	Discharged/ death
1	60, M	HT, DM	Left hemiparesis	5	Right cerebral multiple infarct	Right ICA 75% stenosis	SR, N	LVA	Medical therapy	Discharged
2	77, M	HT, CAD	Aphasia, dysphagia, right hemiplegia	10	Left cerebral multiple infarcts, hemorrhagic transformation in left temporal	Right ICA 75% stenosis, left ICA 30% stenosis	NSR, N	LVA	Medical therapy	Death
3	74, F	AF	Stupor, right hemiplegia	18	Large infarct in the left MCA area	Left MCA M1 occlusion	AF, N	Cardioembolism	Medical therapy	Death
4	60, M	DM	Left upper extremity hemiplegia left lower extremity hemiparesis, left hemihypoesthesia	9	Large infarct in the right MCA area	Right CCA thrombus	NSR, not performed	Undetermined	Mechanical thrombectomy, intravenous heparinization	Discharged
5	79, F	CVD (VST)	Left hemianopia, right-sided ataxia	4	Right cerebellar and occipital infarct	N	NSR, N	Undetermined	Medical therapy	Discharged
6	84, F	HT	Right hemiparesis, motor aphasia	3	Left periventricular infarction	25-50% stenosis on the left and 25% on the right in CCA	NSR, not performed	LVA	Medical therapy	Discharged
7	71, M	HT, DM, CAD, CVD, HF	Right hemihypoesthesia, ataxia	4	Left parietal cortex lacunar infarction	Left ICA 25-50% stenosis	SR, 1st AV block, No thrombus	Lacunar stroke	Medical therapy	Discharged
8	69, M	DM	Confusion, right hemiparesis	6	Left frontal infarction	Left MCA M2 distal stenosis	NSR, not performed	LVA	Medical therapy	Discharged
9	63, F	HT	Left hemiparesis left hemianopia	7	Infarct in the right PCA area	Right PCA P1 distal occlusion	NSR, N	Undetermined	Medical therapy	Discharged
10	55, F	Malignancy	Right hemihypoesthesia, right hemianopia, dysarthria	3	Left parietal and occipital Infarcts	N	NSR, not performed	Undetermined	Medical therapy	Discharged
11	74, F	HT, DM, CAD, HF	Confusion left hemiplegia	14	Infarct in right MCA area	N	ST, No thrombus	Undetermined	Medical therapy	Death
12	81, M	HT, CAD, HF, AF	Confusion aphasia, left hemiparesis and left hemianopia	11	Infarct in right PCA area left subdural hematoma	-	AF, No thrombus, biatrial dilatation, MI, TI	Cardioembolism	Medical therapy	Discharged

Medical therapy: Antiaggregant and/or LMWH or IVH.
NIHSS: National Institutes of Health Stroke Scale, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, AF: Atrial fibrillation, CVD: Cerebrovascular disease, VST: Venous sinus thrombosis, HF: Heart failure, N: Normal, NSR: Normal sinus rhythm, SB: Sinusoidal bradycardia, ST: Sinus tachycardia, MCA: Middle cerebral artery, PCA: Posterior cerebral artery, CCA: Common carotid artery, ICA: Internal carotid artery, MI: Mitral insufficiency, TI: Tricuspid insufficiency, LVA: Large vessel atherosclerosis, M: Male, F: Female, CT: Computed tomography, CTA: CT angiography, CDFI: Color Doppler flow imaging, ECHO: Echocardiography, ECG: Electrocardiogram

(venous sinus thrombosis) (Table 3). LVO was observed after recurrent stroke in patient #10, and both patients were classified as having a stroke of undetermined cause. Patient #5 had a diagnosis of MDS, and, as mentioned above, LMWH was not administered in the first stroke because platelet levels were low.

Discussion

In this study, we examined the demographic characteristics, risk factors, and clinical and laboratory characteristics of patients who developed ischemic stroke associated with SARS-CoV-2 infection. We evaluated the characteristics of stroke patients associated with COVID-19, and the relationship between stroke and COVID-19.

The typical signs and symptoms of COVID-19 infection are fever, cough, and dyspnea. Almost all of our patients developed at least one of these symptoms. While 66.7% of our patients required oxygen during their hospitalization, 75% had a high oxygen required. Intensive care was required in 58.3% of the patients during hospitalization. Studies have reported that SARS-CoV-2 infection causes many neurological signs and symptoms, including stroke, in addition to respiratory ones, and an increased incidence of stroke in patients with severe disease (3,7).

Stroke has emerged as a serious complication of COVID-19. There is a trend toward LVO, multiple infarcts, and involvement of rarely affected vessels in strokes due to COVID-19. However, cerebral vein thrombosis, hemorrhagic infarction, and lacunar infarcts due to small vessel disease are less common (21). In this study, we observed infarcts due to LVO in four patients and lacunar infarction in one patient. The low number of infarcts due to LVO among our patients may be explained by the fact that we did not have a chance to investigate existing occlusion because the pandemic-related conditions restricted us from performing CTA or DSA in some patients.

In the study by Li et al. (22) with 219 patients with COVID-19, 11 patients had a stroke following infection, and the mean age of these patients was 75.7 years. In the same study, it was observed that patients with stroke had risk factors for stroke, such as hypertension, diabetes mellitus, CAD, and prior CVD, and most had severe SARS-CoV-2 infection. In our study, the mean age of the patients was 70.6 years and most patients had severe disease. It was determined that there were risk factors for stroke, such as hypertension and diabetes mellitus, prior CVD, AF, CAD, and malignancy.

In our study, the average D-dimer and IL-6 levels of the patients were high. Hypercoagulability, as evidenced by high D-dimer levels and “cytokine storm” associated with the severity of SARS-CoV-2 infection, may play a role in the pathophysiology of stroke in patients with COVID-19 (8,9). Apart from these factors, the mean age that might cause an increased risk for stroke was high in our patients. Additionally, as mentioned above, vascular risk factors such as hypertension and diabetes mellitus were also commonly observed. More care should be taken in the management of patients with severe COVID-19 and risk factors for stroke, especially in controlling diseases such as hypertension and diabetes mellitus.

In recent studies, the mean time to onset of stroke after symptoms of COVID-19 was similar. In the study of Li et al. (22), this period was 12 days on average. In another study examining six patients with stroke and COVID-19, patients had a stroke on the 10th, 24th, 10th, 2nd, 15th, and 8th days of the onset of COVID-19 symptoms (23). In two other studies in the literature involving large patient groups, the mean time up to the onset of stroke was 10 days (4,24). In our study, the onset of stroke was late, with an average of 10.5 days. This situation is described in the literature as a patient with severe COVID-19 infection possibly developing a prothrombotic state, often complicated by both venous and arterial thromboembolism, following a hyperinflammatory state

Table 4. Analysis of patients with recurrent stroke

Patient no.		Stroke time	Clinical symptoms of ischemic stroke	NIHSS score	CT-MRI stroke location	DSA -CTA-CDFI	D-dimer (mg/L)
5	First stroke	5th day	Left hemianopia, right-sided ataxia	4	Right cerebellar and occipital infarct	N	4.3
	Recurrent stroke	35th day	Left hemianopia, motor aphasia, ataxia	5	Newly developed left frontoparietal and cerebellar multiple infarctions	Not performed	6.3
10	First stroke	21st day	Right hemihypoesthesia, right hemianopia, dysarthria	3	Left parietal and occipital Infarcts	N	9.9
	Recurrent stroke	45th day	Right hemiparesis	5	Newly developed left cerebral and cerebellar multiple infarcts	Left MCA M2 distal occlusion	Not performed

NIHSS: National Institutes of Health Stroke Scale, CT: Computed tomography, CTA: CT angiography, MRI: Magnetic resonance imaging, CDFI: Color Doppler flow imaging

due to a cytokine storm (24). Future studies should focus on the stroke onset time after COVID-19, which may be useful for elucidating the pathophysiology of stroke.

Emergency prophylactic anticoagulation with LMWH is recommended in the literature to prevent a prothrombotic state (25). A study by Shen et al. (26) supported the use of LMWH in patients with COVID-19, especially in older patients with high levels of IL-6, an indicator of hyperinflammatory response, and those with evidence of hypercoagulability (e.g., high D-dimer levels). The international expert panel suggested that LMWH could be started in patients with COVID-19 with suspected cardioembolic stroke or those with low bleeding risk and severe COVID-19 (27).

The Stroke Council of the American Heart Association/ American Stroke Association repeated that all stroke teams should strive to adhere to publish guidelines on patient selection for treatment (28). In an international expert panel review, it was recommended that all eligible patients with stroke should continue to receive intravenous therapy irrespective of their COVID-19 status (27). Mechanical thrombectomy therapy should be offered to all eligible patients regardless of their COVID-19 status (29). However, in a study by Escalard et al. (30), early intravenous thrombolysis and mechanical thrombectomy with successful and rapid recanalization yielded poor outcomes in patients with acute ischemic stroke with COVID-19 due to LVO.

All stroke patients with COVID-19 should be evaluated for prothrombotic and cardioembolic causes, and, accordingly, appropriate secondary prevention should be initiated promptly (29).

Our findings showed that large vessel atherosclerosis, cardioembolic, and lacunar stroke patterns could occur in strokes associated with COVID-19, most patients had severe disease, and the D-dimer level was high, suggesting a hypercoagulable state. This systemic, highly prothrombotic state may facilitate the occurrence of stroke, particularly in patients with cardiovascular risk factors.

Study Limitations

Our study was limited by its retrospective and single-center design and the small number of patients. Additionally, diagnostic tests remained incomplete in some patients due to the pandemic conditions.

Conclusion

These results suggest that COVID-19 triggers stroke rather than being an independent cause and that more care should be taken in the management of patients with risk factors for stroke, and early treatment with LMWH may be beneficial in eligible patients with high D-dimer levels; however, attention should be paid to the risk of hemorrhagic transformation due to LMWH.

Ethics

Ethics Committee Approval: University of Health Sciences Türkiye, Gülhane Faculty of Medicine Ethics Committee (date: 17.06.2021, no: 2021-273).

Informed Consent: This was a retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ü.D., Ö.K., Concept: Ü.D., Ö.K., Design: Ü.D., Ö.K., Data Collection or Processing: Ü.D., Analysis or Interpretation: Ü.D., Ö.K., Literature Search: Ü.D., Writing: Ü.D., Ö.K.

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