Neurology Asia 2025; 30(4) : 987 – 994

Relationship between COVID-19 and stroke: Analysis of biochemical markers and mortality

[1]Bahar Balduz, [2]Metin Balduz, [3]Burak Mete, [4]Tarık Salcan, [3]Ersin Nazlıcan

[1]Directorate of Public Health, Adana, Turkey; [2]University of Health Sciences Adana City Training and Research Hospital, Neurology Department, Adana, Turkey; [3]Cukurova University Faculty of Medicine, Department of Public Health, Adana, Turkey; [4]Directorate of Public Health, Şanlıurfa, Turkey

Abstract

Background & Objective: We aimed to investigate the relationship between COVID-19 and stroke and analyze the biochemical markers that may affect or predict the mortality. *Methods:* This study was conducted at Adana City Training and Research Hospital between March 1, 2020, and December 31, 2020. A total of 220 patients diagnosed with stroke and tested with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) for COVID-19 were included. The patients were divided into two main groups: cerebrovascular disease with negative RT-PCR (CVD) and cerebrovascular disease with positive RT-PCR (CVD+COVID-19). *Results:* COVID-19 patients had a stroke on average at 8.49±6.8 (min:0-max:32) days. Admission to Intensive Care Unit (ICU) rate and mortality rate were significantly higher in CVD+COVID group (92.6% and 57.4% respectively). CVD+COVID-19 group had significantly higher levels of CRP, LDH, PT, INR, aPTT, fibrinogen, procalcitonin, D-Dimer, ferritin, and N/L ratio compared to the CVD group. In CVD-COVID-19 group the risk of admission to ICU increased 4.68 times. Also in this group NIHSS was found to be 20.57±6.19, albumin 33.12±5.23 g/L, and lymphocyte 1.10±0.76 10^3/µl. Higher lymphocyte and albumin and lower NIHSS values are protective effect on mortality and the optimum cut-off value of NIHSS for predicting mortality and admission to ICU are 18.5 (AUC=0.923) and 12.5 (AUC=0.954), respectively. Each 1 unit increase in the NIHSS value increases the risk of admission to ICU and mortality 1.86 times and 1.43 times, respectively.
Conclusion: This study revealed that stroke patients with COVID-19 had a higher risk for mortality and admission to ICU than non-COVID-19. The NIHSS value was a strong predictor for mortality.

Keywords: Stroke, COVID-19, ischemia, NIHSS

INTRODUCTION

COVID-19 is a pandemic that emerged at the end of 2019 and still affects many people worldwide today. Acute respiratory distress syndrome (ARDS), coagulopathy, multi-organ failure and death are the most common complications in severe COVID-19 disease.[1] The incubation period of disease is approximately 5.8 days.[2] The most severe period of the disease is usually between the first 7 -10 days.[3-6] Cytokine storm, one of the most important pathogenesis of the disease, is known to result in the release of rapid and high amounts of proinflammatory cytokines. Releasing of these cytokines and chemokines cause a severe inflammatory pathology in the body with great risks to mortality and morbidity of the patients.[2] Neurological complications, including stroke, movement disorders, motor and sensory deficits, ataxia, and seizures, are common in COVID-19 inpatients.[7] The incidence of cerebrovascular disease in COVID-19 patients is 0.7-5.1%, with the majority of patients having ischemic stroke.[8,9] Altough it is known that COVID-19 is a cause of increasing the incidence of stroke, its effect on prognosis and mortality are not fully understood. The aim of our study is to investigate how COVID-19 affect the mortality of stroke patients.

METHODS

This retrospective study was conducted at the University of Adana City Training and Research Hospital between March 1, 2020-December 31, 2020. All patients who consulted neurology service in the Emergency Department were analysed retrospectively. Ethics committee approval was obtained for the study from

Address correspondence to: Metin Balduz, University of Health Sciences Adana City Training and Research Hospital, Department of Neurology, Adana City Training and Research Hospital, 01060, Yüregir, Adana, Turkey. Tel.: +903224559000-1147 / +905327387453, E-mail: metdical@gmail.com

Date of Submission: 1 August 2023; Date of Acceptance: 30 August 2025

https://doi.org/10.54029/2025nxa

Cukurova University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (decision number 108, dated 12/02/2021).

To calculate the sample size according to the Cohen Guidelines (Cohen's d), the medium size of 0.5 effect size, 0.05 significance and 90% power was chosen, and the minimum sample size to be reached for the intervention group was calculated as at least 172.

In this study the inclusion criteria were: (1) Patients with a nasopharyngeal swab sample, (2) inpatients followed up in the hospital, (3) patients over the age of 18 year, (4) patients with stroke proven by neuroimaging. Exclusion criteria were; (1) patients whose nasopharyngeal swab samples were not taken, (2) outpatients, (3) patients under the age of 18 year, (4) patients missing the parameters for this study, (5) patients who have been transferred to another hospital, (6) patients without stroke proven by neuroimaging.

All patients were divided into two main groups. Those with negative RT-PCR tests were included in cerebrovascular disease (CVD) group. Those with positive RT-PCR tests were included in cerebrovascular disease+COVID-19 (CVD+COVID-19) group.

Each group was further divided into two subgroups; Ischemic stroke: Ischemia, sinüs vein thrombosis (SVT) and transient ischemic attack (TIA) are included; Hemorrhagic stroke: intracerebral hemorrhagic stroke (ICH), subarachnoidal hemorrhagic stroke (SAH), ICH+SAH were included.

The patients diagnosed with stroke were separated, and those who were analyzed with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) tests were included in the study. In addition, RT-PCR test results were searched from hospital database and anamnesis whether if they had COVID-19 before. Glucose, Creatinine, Albumin, CRP, ALT, AST, LDH, PT, INR, aPTT, Fibrinogen, procalcitonin, Troponin, D-Dimer, Ferritin, Leukocyte, Hb, Platelet, Neutrophil, Lymphocyte, and NLR were traced in the patients.

A number of scales are used in order to objectively evaluate the condition of the patients and to reveal their severity. In particular, the NIHSS.[1] It is most commonly used to measure the severity of a stroke and has 11 categories and a score ranging from 0 to 42. The highest score of 42 indicates the most severe and devastating stroke.

The statistical analysis was performed using IBM SPSS Statistics Version 23.0 (IBM, Armonk, NY, USA). Descriptive data were analyzed using frequency distributions expressed as percentages. The Kolmogorov-Smirnov test was used to check the normal distribution of quantitative data. Parametric tests were used for normally distributed data, and non-parametric tests were used for non-normally distributed data. Chi-Square, Independent T, Mann Whitney U, Correlation, and Binary Logistic Regression Analysis tests were used. The significance level was set at $p < 0.05$.

The same independent variables have been used for both mortality and ICU admission. Forward LR method was used in the study. The independent variables of the model were age, gender, comorbid diseases, leukocytes, lymphocytes, hemoglobin, NLR, ferritin, LDH, D-Dimer, ALT, AST, CRP, creatinine, hospitalization time, intensive care hospitalization status, NIHSS and CO-RADS classification. The dependent variable was mortality.

RESULTS

In our study, 6,872 patients who were seen in the Emergency Department and were consulted to the neurology clinic between March 1, 2020 and December 31, 2020 at Adana City Training and Research Hospital were traced, 653 patients were diagnosed with stroke. Due to the absence of PCR testing, incomplete biochemical test results, and referrals to another hospital, only 220 out of the analyzed patients could be included in our study out of a total of 653 patients.There were 141 patients in ischemic CVD group and 61 patients in CVD+COVID-19 group. Comparison data between two groups was given in Table 1.

Biochemical parameters based on patients diagnosed with ischemic stroke were examined and no significant difference was found between CVD group and CVD+COVID-19 group in terms of blood glucose, leukocyte, hemoglobin, blood creatinine, troponin, albumin, AST, ALT platelet and neutrophil levels. However, CRP, LDH, PT, INR, aPTT, fibrinogen, procalcitonin, D-Dimer, ferritin levels and N/L ratio were significantly higher in CVD+COVID-19 group than CVD group (Table 1). NIHSS values were significantly higher in CVD+COVID-19 than CVD group ($p<0.001$).

In this study, all ischemic stroke patients were examined for total hospitalization duration and ICU duration (Table 1). In CVD+COVID-19 group both of the durations were significantly longer ($p<0.001$). The intensive care and mortality rates of the patients were also evaluated in this study. Both rates were significantly longer in CVD+COVID-19 group ($p<0.001$) (Table 2).

Table 1: Group comparison between CVD and CVD+COVID-19 for patients with ischemic stroke

	CVD	CVD+COVID-19	p*
	X±S.D	X±S.D	
Age	67.1±14.6	72.1±13.1	**>0.05**
Stroke day**	-	8.49±6.8	
ICU duration (day)	3.87±7.2	12.06±16.5	**<0.001**
Hospitalization duration (day)	6.9±7.15	15.13±16.2	**0.001**
NIHSS	14.73±7.93	20.57±6.19	**<0.001**
Biochemical parameters			
CRP	39.44±74.79	89.6±94.00	**<0.001**
LDH	278.46±169.67	389.27±	**<0.001**
PT	13.87±11.24	14.41±4.24	**0.003**
INR	1.04±0.26	1.09±0.38	**0.001**
APTT	23.59±3.89	29.86±31.36	**0.017**
Fibrinogen	305.13±179.95	456.31±173.84	**<0.001**
Procalcitonin	3.27±26.10	6.56±18.19	**<0.001**
Troponin	85.28±376.91	337.77±1174.12	**<0.001**
D-Dimer	2284.48±4604.61	4517.06±8997.46	**0.001**
Ferritin	192.80±334.12	813.95±2253.72	**<0.001**
NLR	8.50±20.33	12.75±13.53	**<0.001**
Total	141	61	

*: Independent Sample T Test, CRP: C-reactive protein, LDH: Lactic acid dehidrogenase, PT: Prothrombin time, aPTT: Partial thromboplastin time, INR: International normalized ratio, NLR: Neutrophil/Lymphocyte ratio CVD:Cerebrovascular disease, X: Mean, S.D: Standard deviation

ROC analysis of all ischemic patients were performed to determine the parameters that can be used to predict mortality and admission to ICU. Albumin and lymphocyte levels were intermediate diagnostic tests, and the NIHSS value was a very powerful assessment indicator for mortality (area under the curve 0.923) (Figure 2). The optimum cut-off NIHSS value is 18.5 for the diagnosis of mortality and the sensitivity is 92.8%, the specificity is 85.4%. Predicting to admission to ICU. NIHSS value was a very powerful assessment indicator for ICU (area under the curve 0.954) (Figure 3). The optimum cut-off NIHSS value is 12.5 and the sensitivity is 86.5%, the specificity is 94.7% .

In this study, it was found that the logistic regression analysis created to predict mortality is important. The independent variables of the model were age, gender, comorbid diseases, leukocytes, lymphocytes, hemoglobin, NLR, ferritin,

Table 2: Mortality and intensive care rates in ischemic stroke

		CVD n (%)	CVD+COVID-19 n(%)	p*
ICU	Yes	70 (49.6)	56 (91.8)	**<0.001**
	No	71 (50.4)	5 (8.2)	
Mortality	Yes	34 (24.1)	34 (55.7)	**<0.001**
	No	107 (75.9)	27 (44.3)	
Total		141 (100.0)	61 (100.0)	

*: Chi-Square Test, CVD:Cerebrovascular disease.

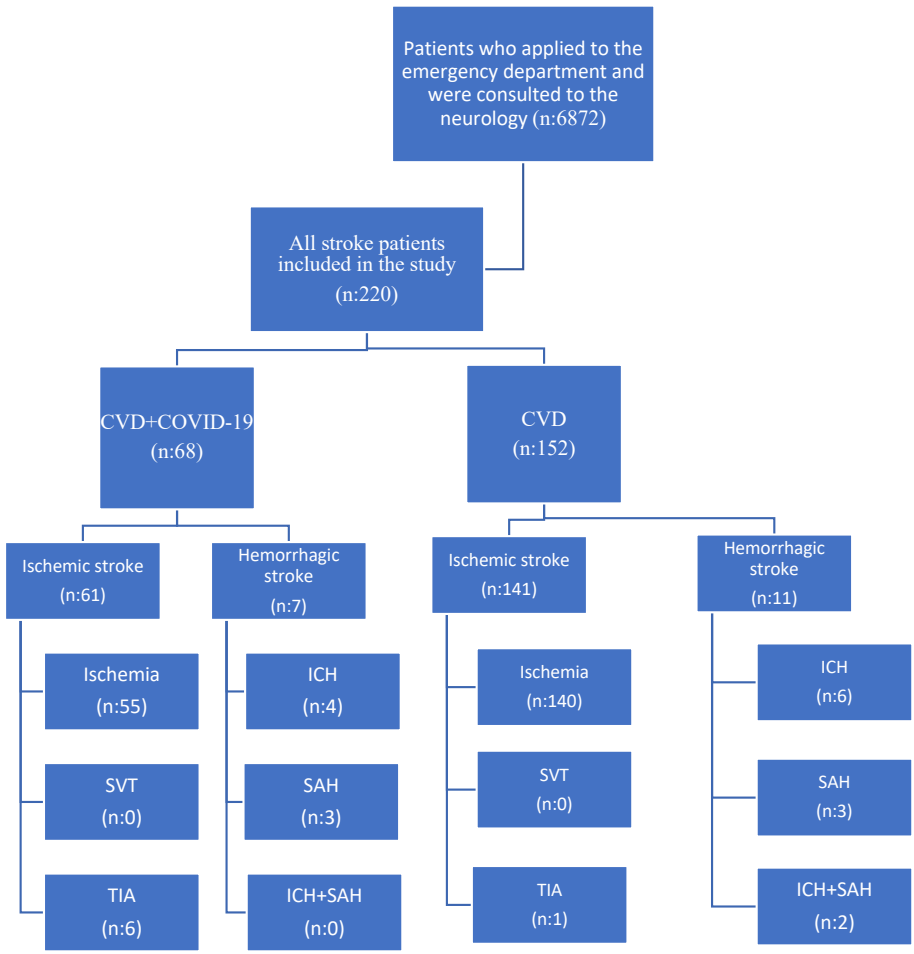

Figure 1. Patient groups

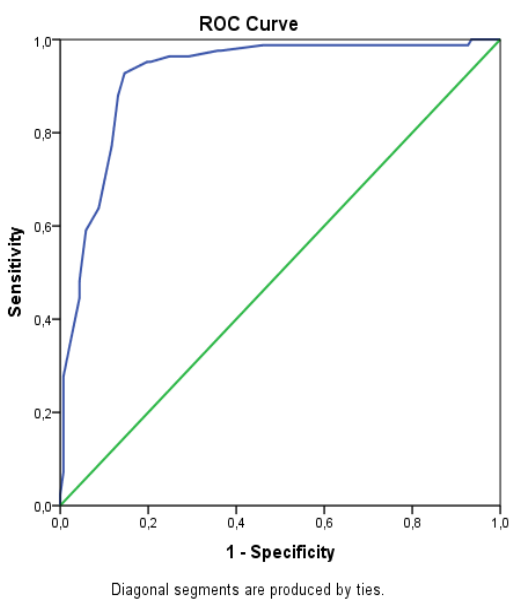

Figure 2. ROC analyse for predicting mortality

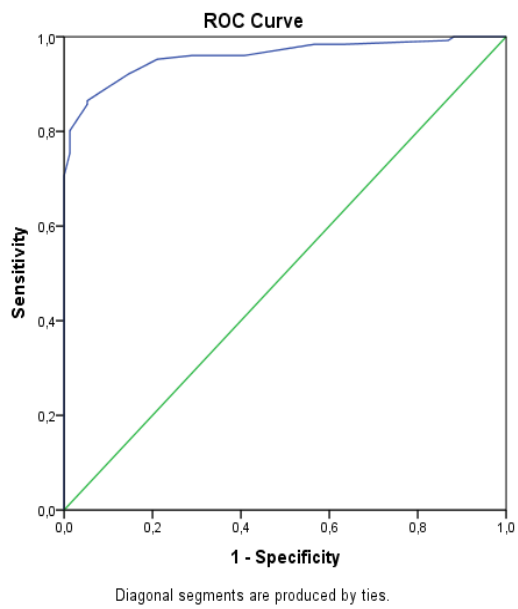

Figure 3. ROC analyse for predicting admission to ICU

LDH, D-Dimer, ALT, AST, CRP, creatinine, hospitalization time, ICU hospitalization status, NIHSS and CO-RADS classification. The dependent variable was mortality. Forward LR method was used in the study. Albumin, NIHSS and lymphocyte parameters were significantly remarkable in the model. Independent variables explain 72.1 percent of the change in dependent variables, and the most important explanatory variable in the model is NIHSS (66%). The most obvious sign is per 1 unit increase in the NIHSS values increases the mortality risk 1.43 times (Table 3).

Logistic regression analysis was found to be important to estimate the rate of intensive care unit admission (Table 3). Albumin, NIHSS and LDH parameters were found to contribute significantly to the model. Independent variables explain 82.5% of the change in dependent variables, and the most important explanatory variable in the model was NIHSS (79%). Per 1 unit increase in albumin levels reduces the risk of intensive care hospitalization by 1.14 times (14%) (OR=0.870), per 1 units in LDH levels increases the risk 1.005 times. The most obvious parameter was NIHSS and per 1 unit increases the risk 1.86 times.

DISCUSSION

Globally, stroke is the third reason of death and the first cause of disability.[2] Incidence of cerebrovascular disease in COVID-19 patients varies between 0.7-5.1% and the majority of cases are ischemic stroke.[3,4] In this study COVID-19 was diagnosed in 30.9% of 220 stroke patients, and 43.2% in ischemic stroke. Katz *et al*, compared 86 patients with COVID-19 and 499 patients with stroke without COVID-19 they found that stroke was an independent risk factor for mortality.[5]

Primarily the main reason of neuronal damage is caused by the systemic inflammatory response triggered by the virus rather than infection. Autopsy studies have not been able to definitively show that the virus directly affects cerebral vessels. However, significant potential evidence was obtained in favor of endothelitis secondary to direct endothelial invasion in organs such as kidney, lung, heart, and liver.[6,7]

In our study the age of ischemic stroke was not a significant difference between the groups. According to the United States stroke registry, the mean age of ischemic stroke is 65[8], the mean age of stroke was 68 year in COVID-19 patients and 71 years in non-COVID-19 stroke patients.[9] In this study we found the age of stroke for our patient was similar to that reported in the literature. Considering the health aspect, elderly ages have a risk in terms of the prognosis of COVID-19. Therefore, early diagnosis and strict isolation of cases over 60 age may be effective in reducing the rate of spread of the infection.

Percentage of the male patients were higher in CVD and CVD+COVID-19 groups but there was no statistical difference between the two groups

Table 3: Logistic regression analysis for ischemic stroke patients

Mortality model					
	B	p	O.R.	95% C.I.	
Parameters				Lower	Upper
Albumin	-0,158	0,003	0,854	0,768	0,949
Lymphocyte	-0,623	0,046	0,536	0,291	0,990
NIHSS	0,363	<0,001	1,437	1,301	1,587
Constant	-1,060	0,549	0,347		
Intensive care unit model					
	B	p	O.R.	95% C.I.	
Parameters				Lower	Upper
Albumin	-0,140	0,042	0,870	0,760	0,995
LDH	0,005	0,012	1,005	1,001	1,010
NIHSS	0,621	<0,001	1,862	1,513	2,291
CVD+COVID	1,540	0,039	4,680	1,083	20,226
Constant	-3,851	0,124	0,021		

CI: Confidence interval NIHSS: National Institutes of Health Stroke Scale

in terms of gender distribution for both men and women. Although stroke is more common in men in most studies[10], in some studies there is no difference according to gender.[11]

In previous studies in ischemic stroke patients, early mortality was commonly associated with high NLR values.[12,13] In the study by Tokgöz *et al*., it was found that increased infarct volume in ischemic stroke was significant for early mortality and NLR showed a positive correlation with infarct volume.[13] The authors suggested that NLR was a predictor for prognosis in ischemic stroke.[12] In our study, the NLR rate was significantly higher in CVD +COVID-19 group than in CVD group for ischemic stroke.

A few studies have shown that there was an association between the risk of first ischemic stroke and CRP levels in healthy individuals.[13-15] However, if CRP levels were evaluated together with vascular risk factors, these levels failed to show the real risk ratio.[14] In our study of ischemic patients, the mean CRP value was significantly higher in CVD+COVID-19 group It is possible to obtain high CRP levels in the inflammatory process peaks, such as COVID-19.

Three large studies indicated that high procalcitonin levels were associated with poor prognostic outcomes.[13] In our study, procalcitonin levels were significantly higher in CVD+COVID-19 group and this result can be associate with COVID-19, which initiates the inflammatory process with many different mechanisms.

It is known that the elevation of ferritin, which is an acute phase reactant in acute infections and tissue damage, is prognostic factor in many cases. It is also recommended to be used in the follow-up of COVID-19. In the study of Chen *et al*., ferritin level was 557.96 (300.78-968.50) ng/mL in patients who survived and 1274.80 (739.57-2000.00) ng/mL in patients who died.[16] In our study, ferritin was significantly higher in the ischemic CVD+COVID-19 group than in the ischemic CVD group. Evidence suggests that severely clinical COVID-19 cases exhibit systemic inflammatory reaction features such as hyperferritinemia.

Although D-Dimer has proven itself most prominently in cancer hypercoagulability, it is also important in increasing the risk of stroke in cardiac embolisms.[19] D-Dimer, which indicates the coagulation state, increases the risk of stroke, as well as anti-cardiolipin antibody levels, inflammatory effects of the virus and endothelial damage by activating thrombotic pathways.[3,4,20] The risk of thrombosis is higher in patients with COVID-19, the risk rises up to 31%, and the risk of pulmonary embolism increases proportionally.[21] It has been reported that high D-Dimer level can be used as a prognostic factor in the early period in severe COVID-19 patient cases.[22] High D-Dimer levels have been associated with a poor prognosis in stroke in many studies.[23] In our study, D-Dimer levels were significantly higher in CVD+COVID-19 group than in CVD group, and a significant increase continued in the ischemic stroke-based comparison. In addition, PT, aPTT, INR and fibrinogen levels, which are another coagulation indicators, were high in the CVD+COVID-19 group. This situation reveals that COVID-19 is an important disease causing coagulopathy.

COVID-19 progressed more seriously in patients with high LDH levels and this condition is correlated with mortality.[24] LDH levels were higher in the patient in intensive care.[25] In our study, LDH levels were significantly higher in the CVD+COVID-19 group and statistically higher in ischemic stroke patients-based comparison.

NIHSS is the parameter that gives the most accurate results in determining the early prognosis of stroke patients.[26] In previous studies NIHSS score was high in COVID-19 patients who had a stroke.[26] In our study NIHSS was significantly higher in the ischemic CVD+COVID-19 group.

Although stroke often occured 1-3 weeks after the onset of COVID-19 symptoms, a small proportion of patients has stroke symptoms at the onset of hospitalization.[5,27-29] Increased inflammation in severe infection causes secondary thrombosis so that the risk for ischemic stroke increases significantly within the first 30 days after hospitalization of these patients.[30]

In this study the mean of ischemic stroke day was 8.49±6.8in patients with COVID-19. Duration of ICU and total hospitalization duration were significantly longer in CVD+COVID-19 group. Considering the hospitalization duration, it can be predicted that COVID-19 will have physical, mental and economic effects.

It has been demonstrated that the NIHSS has a perfect specificity and sensitivity in prognosis assessment.[31] Mortality and disability were proportional with high NIHSS in the previous studies.[31] In another study mortality rate was 34% in strokes with COVID-19 for inpatients.[8] In our study for ischemic stroke patients, mortality rate were 28.9% and 57.4% in CVD group and CVD+COVID-19 group, respectively. Mortality rate was signficantly higher in CVD+COVID-19

group.

In our study albumin, NIHSS and lymphocyte was the most predictor independent paramaterers that could be affect on mortality. In the roc analysis to determine the parameters that can be used to predict the mortality, albumin and lymphocyte levels were intermediate diagnostic tests, but NIHSS score was a very powerful diagnostic test, and the optimum cut-off value we recommend for the diagnosis of mortality is 18.5 for NIHSS. The sensitivity for this value is 92.8%, the specificity is 85.4%.

There were some limitations of this study. Our study was single-centered and hosptial-based. We have not analysed any COVID-19 patients without stroke. Although we searched the objective medical database for a long period and we think that the aim of our study is very important to uncover the causes of stroke that is the most disability disease. Also this study have some Potentials to contribute to science on the effects of COVID-19, which has been declared a pandemic today.

In conclusion, according to the results of our study, the addition of COVID-19 infection in patients with ischemic stroke leads to a worsening of the disease prognosis. COVID-19 positive iscemic stroke patients have higher rates of intensive care unit admissions and mortality. The NIHSS score is a strong predictor for prognosis, and evaluating patients at the time of presentation can be helpful in the management of clinical outcomes.

DISCLOSURE

Conflict of interest: None

REFERENCES

1. Feng GH, Li HP, Li QL, Fu Y, Huang RB. Red blood cell distribution width and ischaemic stroke. *Stroke Vasc Neurol* 2017;2(3):172-5. https://doi.org/10.1136/svn-2017-000071
2. Lloyd-Jones D, Adams RJ, Brown TM, *et al*. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation* 2010;121(7):e46-e215. https://doi.org/10.1161/CIRCULATIONAHA.109.192667
3. Rothstein A, Oldridge O, Schwennesen H, Do D, Cucchiara BL. Acute cerebrovascular events in hospitalized COVID-19 patients. *Stroke* 2020;51(9):e219-e22. https://doi.org/10.1161/STROKEAHA.120.030995
4. Requena M, Olivé-Gadea M, Muchada M, *et al*. COVID-19 and stroke: Incidence and etiological description in a high-volume center. *J Stroke Cerebrovasc Dis* 2020;29(11):105225. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105225
5. Katz JM, Libman RB, Wang JJ, *et al*. Cerebrovascular complications of COVID-19. *Stroke* 2020;51(9):e227-e31. https://doi.org/10.1161/STROKEAHA.120.031265
6. Varga Z, Flammer AJ, Steiger P, *et al*. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020;395(10234):1417-8. https://doi.org/10.1016/S0140-6736(20)30937-5
7. Ackermann M, Verleden SE, Kuehnel M, *et al*. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med* 2020;383(2):120-8. https://doi.org/10.1056/NEJMoa2015432
8. Fridman S, Bres Bullrich M, Jimenez-Ruiz A, *et al*. Stroke risk, phenotypes, and death in COVID-19: Systematic review and newly reported cases. *Neurology* 2020;95(24):e3373-e85. https://doi.org/10.1212/WNL.0000000000010851
9. Srivastava PK, Zhang S, Xian Y, *et al*. Acute ischemic stroke in patients with COVID-19: An analysis from Get With The Guidelines-Stroke. *Stroke* 2021;52(5):1826-9. https://doi.org/10.1161/STROKEAHA.121.034301
10. Dash D, Bhashin A, Pandit AK, *et al*. Risk factors and etiologies of ischemic strokes in young patients: a tertiary hospital study in north India. *J Stroke* 2014;16(3):173-7. https://doi.org/10.5853/jos.2014.16.3.173
11. Ji R, Schwamm LH, Pervez MA, Singhal AB. Ischemic stroke and transient ischemic attack in young adults: risk factors, diagnostic yield, neuroimaging, and thrombolysis. *JAMA Neurol* 2013;70(1):51-7. https://doi.org/10.1001/jamaneurol.2013.575
12. Celikbilek A, Ismailogullari S, Zararsiz G. Neutrophil to lymphocyte ratio predicts poor prognosis in ischemic cerebrovascular disease. *J Clin Lab Anal* 2014;28(1):27-31. https://doi.org/10.1002/jcla.21639
13. Tokgoz S, Keskin S, Kayrak M, Seyithanoglu A, Ogmegul A. Is neutrophil/lymphocyte ratio predict to short-term mortality in acute cerebral infarct independently from infarct volume? *J Stroke Cerebrovasc Dis* 2014;23(8):2163-8. https://doi.org/10.1016/j.jstrokecerebrovasdis.2014.04.007
14. Kaptoge S, Di Angelantonio E, *et al*. C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. *Lancet* 2010;375(9709):132-40. https://doi.org/10.1016/S0140-6736(09)61717-7
15. Ford ES, Giles WH. Serum C-reactive protein and self-reported stroke: findings from the Third National Health and Nutrition Examination Survey. *Arterioscler Thromb Vasc Biol* 2000;20(4):1052-6. https://doi.org/10.1161/01.atv.20.4.1052
16. Chen R, Sang L, Jiang M, *et al*. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. *J Allergy Clin Immunol* 2020;146(1):89-100. https://doi.org/10.1016/j.jaci.2020.05.003
17. Mao R, Qiu Y, He JS, *et al*. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020;5(7):667-78. https://doi.org/10.1016/S2468-1253(20)30126-6

18. Redd WD, Zhou JC, Hathorn KE, *et al*. Prevalence and characteristics of gastrointestinal symptoms in patients with severe acute respiratory syndrome coronavirus 2 infection in the United States: A multicenter cohort study. *Gastroenterology* 2020;159(2):765-7.e2. https://doi.org/10.1053/j.gastro.2020.04.045
19. Montaner J, Perea-Gainza M, Delgado P, *et al*. Etiologic diagnosis of ischemic stroke subtypes with plasma biomarkers. *Stroke* 2008;39(8):2280-7. https://doi.org/10.1161/STROKEAHA.107.505354
20. Merkler AE, Parikh NS, Mir S, *et al*. Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza. *JAMA Neurol* 2020;77(11):1-7. https://doi.org/10.1001/jamaneurol.2020.2730
21. Klok FA, Kruip M, van der Meer NJM, *et al*. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020;191:145-7. https://doi.org/10.1016/j.thromres.2020.04.013
22. Li C, Hu B, Zhang Z, *et al*. D-dimer Triage for COVID-19. *Acad Emerg Med* 2020;27(7):612-3. https://doi.org/10.1111/acem.14037
23. Montellano FA, Ungethüm K, Ramiro L, *et al*. Role of blood-based biomarkers in ischemic stroke prognosis: A systematic review. *Stroke* 2021;52(2):543-51. https://doi.org/10.1161/STROKEAHA.120.029232
24. Henry BM, Aggarwal G, Wong J, *et al*. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. *Am J Emerg Med* 2020;38(9):1722-6. https://doi.org/10.1016/j.ajem.2020.05.073
25. Szarpak L, Ruetzler K, Safiejko K, *et al*. Lactate dehydrogenase level as a COVID-19 severity marker. *Am J Emerg Med* 2021;45:638-9. https://doi.org/10.1016/j.ajem.2020.11.025
26. Kasner SE, Chalela JA, Luciano JM, *et al*. Reliability and validity of estimating the NIH stroke scale score from medical records. *Stroke* 1999;30(8):1534-7. https://doi.org/10.1161/01.str.30.8.1534
27. Lin E, Lantos JE, Strauss SB, *et al*. Brain imaging of patients with COVID-19: Findings at an academic institution during the height of the outbreak in New York City. *AJNR Am J Neuroradiol* 2020;41(11):2001-8. https://doi.org/10.3174/ajnr.A6793
28. Yaghi S, Ishida K, Torres J, *et al*. SARS-CoV-2 and stroke in a New York healthcare system. *Stroke* 2020;51(7):2002-11. https://doi.org/10.1161/STROKEAHA.120.030335
29. Khatana SAM, Groeneveld PW. Health disparities and the coronavirus disease 2019 (COVID-19) Pandemic in the USA. *J Gen Intern Med* 2020;35(8):2431-2. https://doi.org/10.1007/s11606-020-05916-w
30. Elkind MS, Carty CL, O'Meara ES, *et al*. Hospitalization for infection and risk of acute ischemic stroke: the Cardiovascular Health Study. *Stroke* 2011;42(7):1851-6. https://doi.org/10.1161/STROKEAHA.110.608588
31. Jørgensen HS, Reith J, Nakayama H, Kammersgaard LP, Raaschou HO, Olsen TS. What determines good recovery in patients with the most severe strokes? The Copenhagen Stroke Study. *Stroke* 1999;30(10):2008-12. https://doi.org/10.1161/01.str.30.10.2008