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Full Length Article

Racial differences and an increased systemic inflammatory response are seen in patients with COVID-19 and ischemic stroke

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ABSTRACT

Objective: To describe the difference in clinical presentation, including race, of ischemic stroke between patients with and without novel coronavirus disease 2019 (COVID-19), and the association of inflammatory response with stroke severity.

Methods: This is a retrospective, observational, cross-sectional study of patients (n = 60) admitted with ischemic stroke between late March and early May 2020. All patients were tested for COVID-19 during admission. Demographic, clinical, and laboratory data was collected through electronic medical record review. Descriptive statistics was performed to observe the differences between stroke patients with and without COVID-19

Results: 60 hospitalized patients with acute ischemic stroke were included in the analysis. Nine were positive for COVID-19. African-Americans comprised of 55.6% of those that had COVID-19 and stroke and 37.7% of those with only stroke. Stroke patients with COVID-19 had a significantly higher NIHSS [18.4 (8.8)] and neutrophil-to-lymphocyte ratio (NLR) [7.3 (4.2) vs 3.8 (2.8); $P = 0.0137$] than those without. Those with COVID-19 also had a significantly higher mortality rate (44.4% vs. 7.6%; $p < 0.001$).

Conclusion: We observed a cohort of patients, including a large proportion of African-Americans, who developed ischemic stroke with or without COVID-19. An exaggerated inflammatory response, as indicated by NLR, likely plays a role in stroke severity among COVID-19 patients that concurrently develop ischemic stroke.

1. Introduction

In early March 2020, the World Health Organization declared the outbreak caused by the novel coronavirus disease 2019 (COVID-19) as a public health emergency of international concern (Avula et al., 2020). Since then, our knowledge of the clinical phenotype has evolved considerably. Symptoms of COVID-19 go beyond just lung involvement to potentially affecting all organ systems (Huang et al., 2020). More literature have reported COVID-19 impacting the neurologic system, specifically with cerebrovascular disease (Avula et al., 2020; Yaghi et al., 2020; Hess et al., 2020). However, most reports of COVID-19's association with stroke have focused on either how our systems of care have changed (Temporary Emergency Guidance, 2020; Kansagra et al., 2020) or are limited case series reports (Avula et al., 2020; Oxley et al., 2020).

One proposed etiology has been an exaggerated systemic inflammation response to the virus can lead to ischemic stroke, but prior studies have been limited (Yang et al., 2020). The neutrophil to lymphocyte ratio (NLR) is an established inflammation marker of the systemic inflammatory response and is easily calculated from routine blood work by dividing absolute neutrophil count by absolute lymphocyte count (Lagunas-Rangel, 2019; Liu et al., 2020a). Patients with more severe COVID-19 have been shown to have higher NLR, indicating an enhanced inflammatory process that might not be detected with other inflammatory markers (Yang et al., 2020; Lagunas-Rangel, 2019; Liu et al., 2020a). Importantly, racial differences have impacted outcomes of patients with COVID-19 (Ravi, 2020). In this study, we describe the clinical differences, including race, between ischemic stroke patients with and without COVID-19 and laboratory findings including NLR.

2. Methods

This is an observational, cross-sectional study of patients with confirmed acute ischemic stroke between late March to early May 2020 at a single-center urban academic referral hospital in the Southern United

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States. The hospital receives patients from multiple neighboring Southern states. Data was obtained using the center's registry of patients admitted with acute ischemic stroke. The registry received Institutional Review Boards (IRB) approval and followed the standards to protect patients' safety and privacy while gathering clinical information.

Patients (≥18 years) presenting to the center with imaging-verified ischemic stroke during the study period were identified. Electronic medical records were abstracted to confirm stroke cases, and to collect information on: Demographics (age, gender, race), clinical variables (co-existing conditions), laboratory data (complete blood count, blood chemistry, and coagulation tests at admission), and prognostic outcomes (mortality, length of hospital stay, discharge disposition). NLR served as an index of systemic inflammatory response (Yang et al., 2020).

Upon admission, all patients in our cohort were tested for COVID-19 infection similarly to other reported protocols (Avula et al., 2020). Testing for COVID-19 were performed in accordance with standards established by the World Health Organization using reverse-transcriptase polymerase chain reaction from nasopharyngeal swab samples. We categorized our admitted patients with stroke based on COVID-19 status (positive versus negative). Ischemic stroke patients without COVID-19 were our control population.

2.1. Statistical analysis

We calculated descriptive statistics using Wilcoxon two-sample test and Fisher's exact test for continuous and categorical variables, respectively. All analysis was performed using SAS version 9.4 (Cary, USA).

3. Results

A total of 60 hospitalized patients with acute ischemic stroke were included in the analysis, of whom nine were positive for COVID-19 infection. Average age of infected patients was 58.2 ± 18.3 years, three were male, and five were African American. At the time of admission, they presented with a more severe neurological deficit as indicated by a higher NIHSS 18.4 ± 8.8 ($p = 0.04$). Otherwise, past medical history and stroke subtypes were similar between groups. Table 1 reports demographics, clinical variables, laboratory findings, and prognostic outcomes.

3.1. Stroke severity

Patients with NIHSS score higher than 4 also had a significantly high NLR ($p = 0.0069$; not shown in tables). However, prothrombin time ($p = 0.6516$) and partial thromboplastin time ($p = 0.8124$) were not significantly different in patients with high and low NIHSS scores.

3.2. Laboratory findings

Patients with COVID-19 had an increased inflammatory response, including higher neutrophil counts [mean (SD) 76.4 (11.5) vs 66.8 (12.0); $P = 0.0268$], lower lymphocyte count [14.6 (8.8) vs 23.7 (10.3); $P = 0.01$], and increased NLR compared with those patients with no infection [7.3 (4.2) vs 3.8 (2.8); $P = 0.0137$]. Fig. 1 shows an example of a patient with severe COVID-19 infection (NLR = 30.3) and stroke.

3.3. Prognostic outcomes

Stroke patients with COVID-19 had a significantly higher mortality rate (44.4% vs. 7.6%; $p < 0.001$) compared to those without COVID-19. The average length of hospital stay in discharged patients was longer for stroke patients with COVID-19 than those without, but the difference was not clinically significant.

Table 1
Summary of patients with ischemic stroke.

	With Covid-19 (N = 9)	Without Covid-19 (N = 51)	*p*-value
Demographic Characteristics			
Age – yr. (mean ± SD)	58.2 ± 18.3	65.9 ± 13.9	0.25
Male (%)	3 (33.3)	24 (45.3)	0.72
Race (%)			
White	4 (44.4)	29 (58.5)	0.61
African American/Black	5 (55.6)	20 (37.7)	
Other	0 (0.0)	2 (3.8)	
Medical History			
Hypertension (%)	7 (77.8)	46 (90.6)	0.2664
Diabetes (%)	3 (33.3)	19 (35.6)	1.00
Hyperlipidemia (%)	2 (22.2)	28 (52.8)	0.15
History of stroke (%)	1 (11.1)	12 (22.6)	0.67
Atrial Fibrillation (%)	2 (22.2)	13 (24.5)	10,000
Smoking (%)	2 (22.2)	18 (33.8)	0.71
Coronary Artery Disease (%)	0 (0.0)	6 (11.3)	0.58
Congestive heart failure (%)	0 (0.0)	13 (24.5)	0.18
Substance abuse (%)	3 (33.3)	5 (9.4)	0.08
Chronic Kidney Disease (%)	2 (22.2)	6 (11.3)	0.33
DVT/PTE (%)	1 (11.1)	8 (15.1)	1.00
Stroke Information			
NIHSS score on admission (mean ± SD)	18.4 ± 8.8	10.5 ± 8.9	0.04*
Ischemic stroke subtypes			
Large artery (%)	0 (0.0)	10 (18.9)	0.72
Small vessel (%)	1 (11.1)	5 (9.4)	
Cardioembolism (%)	2 (22.2)	11 (20.8)	
Other (%)	1 (11.1)	5 (9.4)	
Cryptogenic (%)	5 (55.6)	22 (41.5)	
Laboratory Values (mean ± SD)			
WBC (4-11 μL)	10.8 ± 6.5	9.1 ± 3.0	0.84
Lymphocytes (15–52 mm^3)	14.6 ± 8.8	23.7 ± 10.3	0.01*
Neutrophils (35–73 mm^3)	76.4 ± 11.5	66.8 ± 12.0	0.03*
NLR	7.3 ± 4.2	3.8 ± 2.8	0.01*
Eosinophils (0–5 cells/mm^3)	2.6 ± 1.3	1.5 ± 1.3	0.04*
Basophils (0–2 cells/mm^3)	0.7 ± 0.5	0.7 ± 0.4	0.85
Monocytes (4–13 cells/mm^3)	5.7 ± 3.1	7.5 ± 2.7	0.07
Hemoglobin (11.3–15.2 g/dL)	10.1 ± 2.6	12.7 ± 2.0	0.01*
Hematocrit (33–45%)	30.1 ± 8.1	38.3 ± 5.8	0.007*
Platelet (150–400 mm^3)	204.3 ± 112.2	233.3 ± 74.8	0.52
Sodium (133–145 mEq/L)	137.4 ± 5.7	137.3 ± 5.0	0.84
Potassium (3.1–5.1 mEq/L)	3.8 ± 0.4	4.1 ± 0.6	0.09
Bicarbonate (22–32 mEq/L)	22.7 ± 4.3	24.6 ± 3.8	0.15
Magnesium (1.7–2.5 mg/dL)	1.8 ± 0.3	2.9 ± 6.2	0.52
Chloride (97–108 mEq/L)	103.6 ± 5.2	103.6 ± 7.5	0.73
Anion Gap (4–16 mEq/L)	11.2 ± 4.5	9.9 ± 2.8	0.61
Glucose (70–100 mg/dL)	125.1 ± 47.7	124.8 ± 69.5	0.56
Blood urea nitrogen (5–22 mg/dL)	20.2 ± 11.4	18.1 ± 9.8	0.63
Serum creatinine (0.4–1.2 mg/dL)	1.1 ± 0.6	1.8 ± 5.2	0.73
Low density lipoprotein (100–130 mg/dL)	73.6 ± 29.3	99.1 ± 37.5	0.07
Hemoglobin A1C %	7.2 ± 2.5	11.3 ± 34.8	0.61
Albumin (3.7–5.5 g/dL)	2.9 ± 0.7	7.5 ± 16.6	0.008*
Prothrombin Time (12–14.5 s)	16.9 ± 3.3	13.9 ± 1.7	0.03*
Activated partial thromboplastin time (25–35 s)	40.9 ± 15.4	29.0 ± 5.2	0.004*
INR	1.4 ± 0.3	1.1 ± 0.2	0.04*
Alkaline phosphatase (37–117 Units/L)[a,b]	89.0 (72.0–106.0)	–	–
Aspartate aminotransferase (12–39 Units/L)[a,b]	49.0 (28.0–96.0)	–	–

(continued on next page)

Table 1 (*continued*)

	With Covid-19 (N = 9)	Without Covid-19 (N = 51)	*p*-value
Alanine aminotransferase (7–52 Units/L)[a,b]	38.0 (11.0–283.0)	–	–
Cardiac Troponin (3–15 ng/L)[a,b]	235.5 (107.0–2147.5)	–	–
Fibrinogen (220–498 mg/dL)[a,b]	207.0 (180.0–1165.0)	–	–
D-Dimer (0–240 ng/mL)[a,b]	2103.5 (1011.5–9973.3)	–	–
C-reactive protein (0–10.9 mg/L)[a,b]	219.8 ± 52.9	–	–
Prognostic Outcomes			
Length of stay for discharged patients[a]	6.0 (4.0–14.0)	3.0 (1.0–6.0)	0.08
Discharge disposition (%)			
Home	1 (11.1)	29 (54.7)	<0.001*
Skilled nursing facility/ subacute rehab	0 (0.0)	5 (9.4)	
Inpatient rehab	0 (0.0)	10 (18.9)	
Transfer to other hospital	2 (22.2)	1 (1.9)	
Deceased	4 (44.4)	4 (7.6)	
Still admitted	2 (22.2)	4 (7.6)	

* p-values<0.05.

Standard deviation (SD), Deep vein thrombosis (DVT), Pulmonary thromboembolism (PTE), The National Institutes of Health Stroke Scale (NIHSS), White blood cells (WBC), Neutrophil-to-lymphocyte ratio (NLR), International normalized ratio (INR).

[a] Values reported as Median (Interquartile range).

[b] Values for stroke patients without Covid-19 not reported due to missing values for more than 20% patients.

4. Discussion

We report important clinical and laboratory differences in ischemic stroke patients with and without COVID-19. To our knowledge, two prior studies have compared these two populations, neither of which addressed racial differences or NLR differences between groups (Yaghi et al., 2020; Ntaios et al., 2020). We report the first experience within the "Stroke Belt" of the Southern United States, which has the highest proportion of African-American stroke patients (Howard et al., 2007). Our cohort had a higher proportion of African-American patients with COVID-19 and stroke than the New York cohort (55.6% vs 15.6%) (Yaghi et al., 2020). This racial disparity could be due to a higher proportion of African American population in the Southeast region compared to other parts of the country. Additionally, the New York cohort did not report their number of African-Americans with stroke who did not have COVID. In our cohort, COVID-19 patients with stroke demonstrated higher severity of neurologic deficit (NIHSS) and a higher mortality rate. These findings were comparable with the New York study which reported a higher median [IQR] NIHSS score: (19 [23] vs 8 [12], $P = 0.007$) and inpatient mortality (63.6% versus 9.3%, $P < 0.001$) among stroke patients with COVID than without (Yaghi et al., 2020). Similarly, Ntaios et al. also reported a significantly higher median NIHSS (10 [4–18] vs 6 [3–14], P = 0.003) and higher mortality (OR = 4.3 [95% CI, 2.22–8.30] among stroke patients with COVID-19 versus without (Ntaios et al., 1208).

The Southern United States has disproportionately higher rates of stroke mortality than the rest of the country (Howard et al., 2007). As COVID-19 has disproportionately burdened African-American communities (Killerby et al., 2020), disparities are likely to widen with other medical conditions (McGonagle et al., 2020) as well that disproportionately affect this community, such as stroke (Cyrus et al., 2020). Additionally, experiences with racial discrimination were associated with elevated cytokine levels in certain African-American groups (Giurgescu et al., 2016). These findings offer an important opportunity to focus education and public health resources on vulnerable populations.

Some studies have suggested the coagulopathy from COVID-19 is caused by a precursor state to disseminated intravascular coagulation (Geng et al., 2020). In our study, we had a small but significant increase in coagulation factors in COVID-19 positive stroke patients compared to those without COVID-19. However, coagulation factors were not independently associated with stroke severity in our study. In contrast, we saw a significantly higher NLR in COVID-19 patients. NLR is a well-studied serum biomarker for systemic inflammation in COVID-19 (Yang et al., 2020; Liu et al., 2020a; Li et al., 2020). The components of the NLR are routinely collected in clinical practice, unlike other systemic inflammatory markers like C-reactive protein and cytokine levels (Lagunas-Rangel, 2019). As part of the complete blood count with differential, the neutrophil count and the lymphocyte count, are already obtained and the ratio can be easily calculated. This would make NLR a cost-effective marker in helping assess disease severity and predict complications (Lagunas-Rangel, 2019).

Interestingly, in our patients with stroke and COVID-19, the neutrophil and lymphocyte levels were only borderline high and low, respectively. Yet, the NLR was almost twice as high as patients without COVID-19. This potentially indicates that the systemic inflammatory response triggered by COVID-19 can cascade from multiple components. *Yang* et al. found that a NLR above the optimum cut-off (3.3) was an independent prognostic biomarker that affected pneumonia progression in COVID-19 patients (Yang et al., 2020). Notably, mean NLR was 7.3 in our study. Increased NLR has also been associated with COVID-19 disease severity, refractory disease, and even an independent factor for mortality (Liu et al., 2020a). Our study is the first study to associate the NLR in patients with COVID-19 and ischemic stroke and stroke severity.

COVID-19 infection likely triggers an exaggerated inflammatory response leading to an excessive production of cytokines or "cytokine storm." (Geng et al., 2020; Liu et al., 2020b) Neutrophils triggered by viral-related cytokines cause tissue damage by release of reactive oxygen species, and inhibit the cytotoxic T-cell response needed to fight viral infection (Yang et al., 2020). Proinflammatory cytokines are known to be increased in COVID-19 patients and associated with disease severity (Geng et al., 2020; Liu et al., 2020c). Subsequent vascular leakage and interstitial edema damage tissues including myocardium and blood vessels (Liu et al., 2020b). A recent study found T-cells were reduced in COVID-19 patients requiring critical care, and these reductions were

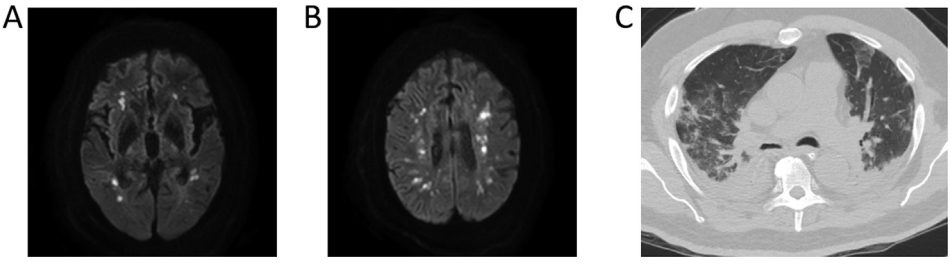

Fig. 1. Example of patient with severe COVID-19(NLP = 30.3)infection and bilateral, multifocal diffusion restriction in the (A) deep white matter structures and (B) subcortices.(C) CT Chest demonstrating large bibasilar consolidations with scattered groundclass opacities with superimposed consolidations.

associated with higher cytokine levels. The authors suggested T-cells were initially hyperactivated and subsequently exhausted in the infection process, impairing anti-viral immunity (Diao et al., 2020). Perhaps the lower circulating lymphocyte counts in our COVID-19 patient cohort was due to reduced T-cells. T-cell lymphocytes are needed to dampen an overactive innate immune response, and subsequent increase of these lymphocytes are seen in disease recovery (Liu et al., 2020c). Prior studies of COVID-19 patients found increased neutrophils are associated with a higher risk of acute respiratory distress syndrome, while lymphopenia has been associated with worse outcomes, increased need for critical care, and increased mortality (Terpos et al., 2020). Medications that can block the systemic inflammatory response such as Dexamethasone, a corticosteroid, have had early reports that suggest improved outcomes due to its ability to suppress neutrophils (Horby et al., 2020). African-Americans have known genetic variations associated with inflammation measured using the NLR and increased risk of cardiovascular disease and stroke (Angkananard et al., 2019; Kim et al., 2018). In these populations who receive medications like dexamethasone, it will be important to monitor the differences in their medications effects.

Our study has several limitations. First, this was a retrospective, observational single-center study with a small sample size, which limited our ability to perform multivariable statistical analysis. Secondly, even though overall our cohort had a large proportion of African American population, within the COVID-19 group, the absolute difference in the numbers of African American patients versus other race was one. Therefore, the results of this report should be interpreted with caution. Third, not all patients had the same completeness of laboratory data and so some comparisons could not be made. Fourth, we do not have all prognostic outcomes since some patients were still admitted and receiving clinical care. Finally, we did not study hemorrhagic stroke, which warrants further investigation.

5. Conclusion

We observed a cohort of patients including a large proportion of African-American population, who developed ischemic stroke with or without COVID-19. Those with COVID-19 and ischemic stroke had higher stroke severity and increased mortality. We also found that an increased NLR among stroke patients with COVID-19 indicates a more severe systemic inflammatory response that impacts clinical characteristics and warrants further investigation.

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Disclosures

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Declaration of competing interest

The authors have no Conflicts of interests to declare.

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References

Angkananard, T., Anothaisintawee, T., Ingsathit, A., et al., 2019. Mediation effect of neutrophil lymphocyte ratio on cardiometabolic risk factors and cardiovascular events. Sci. Rep. 9 (1), 2618-2618.

Avula, A., Nalleballe, K., Narula, N., et al., 2020. COVID-19 presenting as stroke. Brain Behav. Immun. 87, 115–119.

Cyrus, E., Clarke, R., Hadley, D., et al., 2020. The impact of COVID-19 on African American communities in the United States. Preprint. medRxiv. https://doi.org/10.1101/2020.05.15.20096552. Published 2020 May 19.

Diao, B., Wang, C., Tan, Y., et al., 2020. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). Front. Immunol. 11.

Geng, Y.-J., Wei, Z.-Y., Qian, H.-Y., Huang, J., Lodato, R., Castriotta, R.J., 2020. Pathophysiological characteristics and therapeutic approaches for pulmonary injury and cardiovascular complications of coronavirus disease 2019. Cardiovasc. Pathol. 47, 107228.

Giurgescu, C., Engeland, C.G., Templin, T.N., Zenk, S.N., Koenig, M.D., Garfield, L., 2016. Racial discrimination predicts greater systemic inflammation in pregnant African American women. Appl. Nurs. Res. 32, 98–103.

Hess, D.C., Eldahshan, W., Rutkowski, E., 2020. COVID-19-Related stroke. Translat. Stroke Res. 11, 322–325.

Horby, P., Lim, W.S., Emberson, J., et al., 2020. Effect of dexamethasone in hospitalized patients with COVID-19: preliminary report. medRxiv, 2020.2006.2022.20137273.

Howard, G., Labarthe, D.R., Hu, J., Yoon, S., Howard, V.J., 2007. Regional differences in African Americans' high risk for stroke: the remarkable burden of stroke for Southern African Americans. Ann. Epidemiol. 17 (9), 689–696.

Huang, C., Wang, Y., Li, X., et al., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395 (10223), 497–506.

Kansagra, A.P., Goyal, M.S., Hamilton, S., Albers, G.W., 2020. Collateral Effect of Covid-19 on Stroke Evaluation in the United States. New England Journal of Medicine 383 (4), 400–401.

Killerby, M.E., Link-Gelles, R., Haight, S.C., et al., 2020. Characteristics associated with hospitalization among patients with COVID-19 - metropolitan atlanta, Georgia, march-april 2020. MMWR Morb. Mortal. Wkly. Rep. 69 (25), 790–794.

Kim, S., Eliot, M., Koestler, D.C., Wu, W.-C., Kelsey, K.T., 2018. Association of neutrophil-to-lymphocyte ratio with mortality and cardiovascular disease in the jackson heart study and modification by the duffy antigen variant. JAMA cardiology 3 (6), 455–462.

Lagunas-Rangel, FA., 2020. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. J. Med. Virol. Published on April 03.

Li, Y., Li, M., Wang, M., et al., 2020. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke and Vascular Neurology. https://doi.org/10.1136/svn-2020-000431.

Liu, Y., Du, X., Chen, J., et al., 2020a. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J. Infect. 81 (1), e6–e12.

Liu, J., Zheng, X., Tong, Q., et al., 2020b. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERS-CoV, and 2019-nCoV. J. Med. Virol. 92 (5), 491–494.

Liu, J., Li, S., Liu, J., et al., 2020c. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine 55, 102763.

McGonagle, D., Plein, S., O'Donnell, J.S., Sharif, K., Bridgewood, C., 2020. Increased cardiovascular mortality in African Americans with COVID-19. Lancet Respir Med 8 (7), 649–651.

Ntaios, G., Michel, S., Georgiopoulos, J., et al., 2020. Characteristics and Outcomes in Patients With COVID-19 and Acute Ischemic Stroke. Stroke 51 (9), e254–e258.

Oxley, T.J., Mocco, J., Majidi, S., et al., 2020. Large-vessel stroke as a presenting feature of covid-19 in the young. N. Engl. J. Med. 382 (20), e60.

Ravi, K., 2020. Ethnic disparities in COVID-19 mortality: are comorbidities to blame? Lancet (London, England) 396 (10243), 22-22.

Temporary Emergency Guidance to US Stroke Centers During the Coronavirus Disease 2019 (COVID-19) Pandemic. Stroke 51 (6), 2020, 1910–1912.

Terpos, E., Ntanasis-Stathopoulos, I., Elalamy, I., et al., 2020. Hematological findings and complications of COVID-19. Am. J. Hematol.

Yaghi, S., Ishida, K., Torres, J., et al., 2020. SARS-CoV-2 and stroke in a New York healthcare system. Stroke 51 (7), 834–847, 95.

Yang, A.-P., Liu, J.-P., Tao, W.-Q., Li, H.-M., 2020. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int. Immunopharm. 84, 106504-106504.