ORIGINAL ARTICLES

Influence of the COVID-19 pandemic on acute stroke care. Experience of a comprehensive stroke center in Bulgaria

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Abstract

Background & Objectives: The coronavirus disease 2019 (COVID-19) pandemic had a significant impact on clinical practice worldwide with severe consequences for acute stroke care. We aimed to evaluate our institution's experience and measure the impact of the COVID-19 pandemic on acute stroke care in a single-center in Varna, Bulgaria. *Methods:* We conducted a retrospective study, including all the patients presented with acute stroke to a tertiary care referral center for neurological disorders in Eastern Bulgaria. We compared the data about stroke incidence, patient characteristics, treatment details, logistics, mortality rate, and general qualitative parameters in two periods - July to September 2020 (COVID) and the corresponding period in 2019 (pre-COVID). *Results:* There was a 17.29% increase in all admissions in the COVID period compared with 2019, as there were more patients with first-ever ischemic stroke (p=0.031) and more severe cases in comatose state during admission (p=0.0001). During the pandemic, the time from onset to arrival in the hospital was significantly prolonged from 231 ± 233 minutes in 2019 to 615 ± 1179 minutes (p=0.0001), intravenous thrombolysis rates were decreased (p=0.014), mortality from acute ischemic stroke was two-fold higher, and stroke-survivors had a higher disability (p=0.0001). A decrease in the rehabilitation assessment was noted (p=0.002), while door-to-needle time for thrombolysis and other major qualitative parameters of acute stroke care did not significantly differ.
Conclusion: During the COVID pandemic, we found an increase in stroke cases and a substantial delay from stroke onset to hospital presentation. These logistics changes could be one reason that led to more severe cases with worse functional outcomes and higher mortality rates.

Keywords: Stroke, ischemic stroke, COVID-19, thrombolysis, intravenous thrombolysis, mortality, RES-Q database, comprehensive stroke center, Balkan region, Bulgaria

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic generated a significant burden on healthcare systems worldwide. There are severe consequences in managing all medical emergencies, in particular cardiovascular conditions, and acute stroke patients' care.[1] The exact relationship between cerebral stroke and COVID-19 is not fully clear yet.[2] Nevertheless, the COVID-19 infection induces a hyper coagulant state and increases the risk of thromboembolic events, including stroke, and it is now considered an independent risk factor for acute ischemic stroke.[3-5]

Divergent data is present regarding stroke incidence during the pandemic depending on the country and the specific local healthcare regulations. Some authors report a rising incidence of an acute stroke[4,6,7], while others state a decline in the cases presenting with acute stroke.[8-11]

Nevertheless, there is a consensus that the COVID-19 pandemic leads to a significantly

increased delay from the stroke onset to the hospital admission of stroke patients, resulting in a rising number of patients presenting outside of the time-sensitive treatment windows.[10,12,13] During the COVID-19 period, there is a decrease in the timely diagnosed ischemic stroke cases, which further leads to a decrease in intravenous thrombolysis (IVT) rates.[14]

Our study aims to evaluate our institution's experience with patients presenting with symptoms of acute stroke during the COVID-19 pandemic and assess its impact on the number of hospitalized stroke patients, patient characteristics, and general qualitative parameters in Varna, Bulgaria.

METHODS

We conducted a retrospective observational study including all the patients presented with acute stroke to Second Clinic of Neurology with ICU and stroke unit at the University Hospital St. Marina in Varna Bulgaria. This clinic is a tertiary care referral center for neurological disorders and the largest one providing differentiated treatment of acute stroke patients, including thrombolysis and mechanical thrombectomy, in Eastern Bulgaria.

We compared the data from the registry of stroke care quality (RES-Q) registry of two time periods. The first period involved the third quarter (Q3) of 2019 from July to September, representing the situation before the COVID-19 pandemic. The second one was from the Q3 period of 2020 during the pandemic.

We analyzed the incidence of different stroke subtypes, stroke severity, time from stroke onset to arrival in the hospital, administered intravenous thrombolysis (IVT) as a specialized acute ischemic stroke (AIS) treatment, and stroke mortality cases during the two periods.

All the data was obtained from the RES-Q registry, as we did a cross-referencing with data from our center to check for missing cases and information. The statistical analysis included descriptive and inferential statistics. A comparison of means was made using the ANOVA test, while the comparison of proportions was made with Fisher's exact test. Statistical significance was defined as a P-value (alpha) of 0.05 or less.

Data were analyzed using the software programs SPSS, version 23.00 (IBM Statistics, USA) and GraphPad Prism, version 5.00 (GraphPad Software, San Diego California, USA).

RESULTS

A total of 312 patients presented with acute stroke symptoms during the Q3-2020 COVID period and 266 during the Q3-2019 pre-COVID control period. The percentage increase between the number of patients in both periods represents a 17.29% increase in all admissions. There were no significant differences in the distribution of stroke subtypes (Table 1).

Focusing on the patients with acute ischemic stroke (AIS), we found a mean age of 70.73 ± 11.86 in Q3-2019 and 71.25 ± 11.40 in Q3-2020. There were no significant differences in sex distribution.

During the COVID period, there is a rise of first-ever ischemic stroke cases (p=0.031). The mean presenting NIHSS score was slightly higher, 10.22 ± 7.47 in 2020, compared to 9.35 ± 6.59 during the pre-COVID period (p=0.173). The proportion of the severe ischemic stroke cases was higher in 2020 – 10.8% compared to 6.6% in 2019, but without statistical significance (p=0.116). Nevertheless, in the proportion of ischemic stroke patients in comatose state was significantly higher in Q3-2020 (p=0.0001). Notably, the proportion of patients with known last-known-well (LKW) time is higher in the COVID period 43.2% compared to 35.8% in 2019 (p=0.101), but yet fewer patients were hospitalized in the therapeutic window for intravenous thrombolysis – 21.5% in Q3-2020 and 26.6% in Q3-2019 (p=0.209).

The mean time from last-known-well (LKW) to arrival in the hospital was significantly longer in Q3-2020 - 615 ± 1179 minutes, while in Q3-2019, it was 231 ± 233 minutes (p=0.0001). The rate of performed intravenous thrombolysis was significantly decreased – 5.4% in Q3-2020 in contrast with 11.8% in the pre-COVID period (p=0.014). Door-to-needle time (DTN) was decreased from 78.26 ± 33.32 in 2019 to 67.27 ± 27.34 during the COVID pandemic, without reaching statistical significance (p=0.282).

The primary qualitative parameters of acute stroke care did not present with significant differences, except for a decrease in the proportion of patients who have been screened for rehabilitation in the first 24 hours during the COVID period (p=0.003).

There was a rise in the mortality rates from an acute ischemic stroke from 17.0% in Q3-2019 up to 32.0% in Q3-2020 (p=0.0001). There were also fewer patients discharged to social facilities (p=0.006).

Table 1: Distribution of stroke subtypes in Q3 2019 in comparison to Q3 2020 according to the RES-Q database

Parameter	Q3-2019 (July-September)	Q3-2020 (July-September)	P-value
Total stroke patients	266	312	+17.29%
Ischemic stroke *(IS)*	229 (86.1%)	278 (89.1%)	0.151
Transient ischemic attack *(TIA)*	0 (0.0%)	1 (0.3%)	0.372
Intracerebral hemorrhage *(ICH)*	33 (12.4%)	27 (8.7%)	0.147
Subarachnoid hemorrhage *(SAH)*	2 (0.8%)	5 (1.6%)	0.385
Cerebral venous thrombosis *(CVT)*	2 (0.8%)	1 (0.3%)	0.410

The mean disability rates showed an increase reaching 2.19 ± 1.43 in the COVID period compared to 1.58 ± 1.59 during the control period (p=0.0001). The proportions of functionally dependant and independent patients on discharge did not differ.

Detailed information about the demographics and qualitative parameters of acute stroke care during the COVID period and the pre-COVID control period are presented in Table 2.

DISCUSSION

We observed a 17.29% increase in the number of all patients presented with acute stroke symptoms to our center during the COVID-19 pandemic. We found a delayed presentation of stroke patients to the hospital in 2020 in comparison to 2019. Fewer cases were presented in the first 4.5 hours time window from stroke onset when intravenous thrombolysis can be administered for well-selected patients. These delays resulted in a significant decrease in the rate of performed intravenous thrombolysis, while the door-to-needle time (DTN) remained without significant change between the two periods. Interestingly, the initial NIHSS was similar between the two time periods, while the functional outcomes were much worse during the Q3-2020. The average level of disability was significantly higher during the COVID-19 pandemic period, and there was a significant increase in mortality - up to twice as much as in the control period.

Various factors affect the changes in stroke presentation during the COVID-19 pandemic. Patients might be unwilling to look for emergency medical services or go to the hospital during the pandemic due to fear of contact with COVID-19, which leads to late presentation and more severely symptomatic. Additionally, patients with mild stroke or transient ischemic attacks may avoid the healthcare system and undergoing no or ineffective treatment, which is very dangerous in the sense of recurrent ischemic stroke and inadequate secondary prevention.[15] It can be concluded from our results that exceptions are made in severe disabling stroke cases when there is a lack of treatment options at-home. There is also a growing proportion of cases found by others with incapacitating stroke from medical history, maybe due to the social distancing measures. One possible explanation for the growing number of stroke cases in our center might be local regulations and restrictions. Various wards where stroke patients were treated in the pre-COVID-19 period were transformed into specific wards to treat COVID-19 infection during 2020.

Nevertheless, more patients present to the hospitals with a severe delay from the first stroke symptoms.[10,11] The longer time from onset to hospitalization restricts patients from meeting the criteria for life-saving differentiated treatment options such as intravenous thrombolysis.[10] Conclusively, there is growing mortality in stroke patients due to the late hospital presentation and higher disability rates in stroke survivors. We found a decrease in the rehabilitation assessments, while the two main reasons were the patients' uncertain COVID-19 status and many patients with febrile conditions that are contraindicated for acute rehabilitation. It should be noted that the major in-hospital qualitative parameters, such as neuroimaging on admission, dysphagia screening, and the door-to-needle time (DTN), were not affected during the COVID-19 period. These findings prove our stroke center's readiness to provide timely and complete care in acute ischemic stroke in a pandemic situation.

Various guidelines and informational campaigns for patients were made in the last months to ensure high-quality stroke care in all stroke centers worldwide.[16-18] Nevertheless, each country has a specific healthcare system and local difficulties

Table 2: Demographics and qualitative parameters of acute ischemic stroke care in Q3 2019 in comparison to Q3 2020 according to the RES-Q database

Parameter	Q3-2019 (July-September)	Q3-2020 (July-September)	P-value
Characteristics of the patients with acute ischemic stroke			
Age	70.73 ± 11.86	71.25 ± 11.40	0.616
Female	115 (50.2%)	127 (45.7%)	0.326
First-ever stroke	155 (67.7%)	212 (76.3%)	**0.031**
Recurrent stroke	74 (32.3%)	66 (23.7%)	**0.031**
Stroke Severity measured by NIHSS			
Mean NIHSS	9.35 ± 6.59	10.22 ± 7.47	0.173
Mild (*NIHSS 1-4*)	68 (29.7%)	72 (25.9%)	0.370
Moderate (*NIHSS 5-15*)	110 (48.0%)	144 (51.8%)	0.422
Moderate-to-severe (*NIHSS 16-20*)	36 (15.7%)	32 (11.5%)	0.191
Severe (*NIHSS ≥ 21*)	15 (6.6%)	30 (10.8%)	0.116
Level of consciousness measured by GLCS			
Alert	168 (73.4%)	178 (64.0%)	**0.024**
Drowsy	45 (19.7%)	68 (24.5%)	0.197
Comatose	5 (2.2%)	32 (11.5%)	**0.0001**
Parameters and mean times regarding the intravenous thrombolysis			
Patients with known LKW time	82 (35.8%)	120 (43.2%)	0.101
Hospitalization in 4.5h from onset	61 (26.6%)	60 (21.6%)	0.209
Time from onset to hospitalization (min)	231 ± 233	615 ± 1179	**0.0001**
Performed intravenous thrombolysis	27 (11.8%)	15 (5.4%)	**0.014**
DTN	78.26 ± 33.32	67.27 ± 27.34	0.282
Qualitative parameters of acute stroke care			
Hospitalized in Stroke Unit	229 (100.0%)	275 (98.9%)	0.112
NIHSS performed on admission	229 (100.0%)	278 (100.0%)	1.000
CT/MRI performed on admission	229 (100.0%)	276 (99.3%)	0.504
Vascular imaging	81 (35.3%)	88 (31.7%)	0.395
Dysphagia screening (Guss test)	228 (99.6%)	272 (97.8%)	0.135
Patients assessed for rehabilitation	228 (99.6%)	272 (97.8%)	0.135
Rehabilitation assessment < 24h hours	227 (99.13%)	262 (94.24%)	**0.003**
Mean hospital stay	6.65 ± 6.49	6.89 ± 5.39	0.646
Discharge destination			
To own home	151 (66.0%)	165 (59.4%)	0.141
To social facility	39 (17.0%)	24 (8.6%)	**0.006**
Discharged due to death	39 (17.0%)	89 (32.0%)	**0.0001**
Level of disability measured by mRS on discharge			
Mean mRS	1.58 ± 1.59	2.19 ± 1.43	**0.0001**
Functional independence (*mRS 0-2*)	128 (67.4%)	125 (66.1%)	0.828
Functional dependency (*mRS 3-5*)	62 (32.6%)	64 (33.9%)	0.828

NIHSS = National Institutes of Health Stroke Scale; GLCS = Glasgow-Liège Coma Scale; mRS = modified Rankin Scale; LKW = Last known well; DTN = Door-to-Needle time;

and regulations. Therefore, it is impossible to develop and follow a single stroke care model in a pandemic situation. There is an utmost need to raise awareness of the patients not to wait too long at home in case of a medical emergency. In particular, patients with acute onset of even mild and non-disabling symptoms of stroke must not stay at home but call for emergency medical care so that they can take advantage of the modern treatments for acute stroke.[19] By following these recommendations, we would be able to achieve our main goals - to reduce stroke mortality and to decrease the disability in stroke-survivors.

Our study has several limitations. First, data collection was retrospective, covering the period only for the third quarter of 2019 and 2020. Second, we report a local single-center experience, so it is not generalizable, and it is unknown if the COVID-19 pandemic had a similar effect on other stroke centers. Finally, we are not reporting data on long-term functional outcomes in this study. Future studies may address this, ideally using data from national or international collaborations, which may lead to more clearance in the long-term influence of the COVID-19 pandemic on acute stroke care.

In conclusion, we found an increase in the number of stroke cases, a substantial delay from stroke onset to hospital presentation These logistics changes could be one reason that led to more severe cases with worse functional outcomes and higher mortality rates during the COVID-19 pandemic, while there was no evidence for a change in the quality of acute stroke care in Varna, Bulgaria.

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DISCLOSURE

Conflict of interest: None

REFERENCES

1. Rinkel L, Prick J, Slot R, *et al*. Impact of the COVID-19 outbreak on acute stroke care. *J Neurol* 2020:1-6.
2. Wang Z, Yang Y, Liang X, *et al*. COVID-19 associated ischemic stroke and hemorrhagic stroke: Incidence, potential pathological mechanism, and management. *Front Neurol* 2020;11:571996.
3. Lee KW, Khan AHKY, Ching SM, *et al*. Stroke and novel coronavirus infection in humans: A systematic review and meta-analysis. *Front Neurol* 2020 Oct 6;11:579070.
4. Kolikonda MK, Jandrasupalli KK, Lippmann S. Association of coronavirus disease 2019 and stroke: A rising concern. *Neuroepidemiology* 2020;54(5):369-73.
5. Fifi JT, Mocco J. COVID-19 related stroke in young individuals. *Lancet Neurol* 2020;19(9):713-5.
6. Requena M, Olivé-Gadea M, Muchada M, *et al*. COVID-19 and stroke: Incidence and etiological description in a high-volume center. *J Stroke Cerebrov Dis* 2020;29(11):105225.
7. Modin D, Claggett B, Sindet-Pedersen C, *et al*. Acute COVID-19 and the incidence of ischemic stroke and acute myocardial infarction. *Circulation* 2020;142(21):2080-2.
8. Zhao J, Rudd A, Liu R. Challenges and potential solutions of stroke care during the coronavirus disease 2019 (COVID-19) outbreak. *Stroke* 2020;51(5):1356-7.
9. Siegler JE, Heslin ME, Thau L, Smith A, Jovin TG. Falling stroke rates during COVID-19 pandemic at a comprehensive stroke center. *J Stroke Cerebrov Dis* 2020;29(8):104953.
10. Nagamine M, Chow DS, Chang PD, Boden-Albala B, Yu W, Soun JE. Impact of COVID-19 on acute stroke presentation at a comprehensive stroke center. *Front Neurol* 2020;11(850).
11. Morelli N, Rota E, Terracciano C, *et al*. The baffling case of ischemic stroke disappearance from the casualty department in the COVID-19 era. *Eur Neurol* 2020;83(2):213-5.
12. Montaner J, Barragán-Prieto A, Pérez-Sánchez S, *et al*. Break in the stroke chain of survival due to COVID-19. *Stroke* 2020;51(5):1356-7.
13. Markus HS, Brainin M. COVID-19 and stroke—A global World Stroke Organization perspective. *Int J Stroke* 2020;15(4):361-4.
14. Ortega-Gutierrez S, Farooqui M, Zha A, *et al*. Decline in mild stroke presentations and intravenous thrombolysis during the COVID-19 pandemic: The Society of Vascular and Interventional Neurology Multicenter Collaboration. *Clin Neurol Neurosurg* 2020:106436.
15. Dula AN, Brown GG, Aggarwal A, Clark KL. Decrease in stroke diagnoses during the COVID-19 pandemic: Where did all our stroke patients go? *JMIR Aging* 2020;3(2):e21608.
16. Wira CR, Goyal M, Southerland AM, *et al*. Pandemic guidance for stroke centers aiding COVID-19 treatment teams. *Stroke* 2020;51(8):2587-92.
17. Dafer RM, Osteraas ND, Biller J. Acute stroke care in the coronavirus disease 2019 pandemic. *J Stroke Cerebrov Dis* 2020; 29(7):104881.
18. Aguiar de Sousa D, van der Worp HB, Caso V, *et al*. Maintaining stroke care in Europe during the COVID-19 pandemic: Results from an international survey of stroke professionals and practice recommendations from the European Stroke Organisation. Eur Stroke J 2020:5(3):230-6.
19. Deerberg-Wittram J, Knothe C. Do not stay at home: We are ready for you. *NEJM Catal Innov Care Deliv* 2020:10.1056/CAT.20.0146.