



Stringent public health measures during COVID-19 across ischemic stroke care systems: the potential impact of patient perceptions on health care-seeking behaviors

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Abstract Decreases in acute stroke presentations have been reported during the coronavirus disease 2019 (COVID-19) pandemic surges. A recent study by Bojti et al. (*GeroScience*. 2021;43:2231–2248) sought to understand the relationship of public health mandates in Hungary as they were implemented with acute ischemic stroke admissions and interventions during two separate COVID-19 waves. We sought to perform a similar analysis of changes in ischemic stroke care at two distinct medical institutions in the USA. Two separate institutions and systems of ischemic stroke care were evaluated through a regional comprehensive stroke center telestroke service

and a Veterans Affairs (VA) inpatient stroke and neurorehabilitation service. Telestroke consultations in a single system in Chicago, IL, were significantly decreased during the first COVID-19 wave during severely restricted public health mandates (z -score < -2), and were less depressed during a subsequent wave with less severe restrictions (z -score approaching -1), which resembles findings in Hungary as reported by Bojti et al. In contrast, inpatient admissions during the first and second COVID-19 waves to a VA stroke and neurorehabilitation service in Oklahoma City remained unchanged. The Chicago and Hungary patterns of stroke presentations suggest

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that public perceptions, as informed by regional health mandates, might influence healthcare-seeking behavior. However, the VA experience suggests that specific patient populations may react differently to given public health mandates. These observations highlight that changes in stroke presentation during the COVID-19 pandemic may vary regionally and by patient population as well as by the severity of public health mandates implemented. Further study of COVID-19-related public health policies on acute stroke populations is needed to capture the long-term impact of such policies. Learning from the real-time impact of pandemic surges and public health policy on presentation of acute medical conditions, such as ischemic stroke, may prove valuable for designing effective policies in the future.

Keywords Acute stroke population · COVID-19 · Health care behaviors · Public health policy

Introduction

Since early in the coronavirus disease 2019 (COVID-19) pandemic, there have been anecdotal reports from around the globe of reduced presentations and hospitalizations for stroke and other acute medical conditions, including myocardial infarction. These reduced presentations occurred despite an increased risk for both acute thrombotic events [1–4] and intracranial hemorrhages [5–7] in patients with COVID-19. The SARS-CoV-2 virus can infect the vascular endothelial cells, which abundantly express ACE-2 (angiotensin-converting enzyme-2) [8–10], the entry receptor of the virus. There is increasing evidence causally linking SARS-CoV-2 infection to both microvascular and macrovascular pathologies, resulting in a wide range of neurological consequences, from development of multiple cerebral microhemorrhages and lacunar infarcts [11–14] to larger ischemic strokes [3, 4] and intracerebral hemorrhages [5–7].

After the first wave of COVID-19 (spring 2020) subsided in various regions around the world, these anecdotal reports of reduced acute presentations for stroke were confirmed by multiple separate groups [15–19]. The recent publication by Bojti et al. [20] in *Geroscience* is unique among these reports in that they provide additional insight by presenting specific data from several years of pre-pandemic

acute stroke admissions, cases from multiple consecutive COVID-19 waves, and corresponding public health mandates that were implemented in an effort to mitigate COVID-19 associated morbidity. The national scope of these data suggests that the study results and potential public health lessons are likely to generalize to similar socioeconomic settings outside of Hungary, where Bojti et al. [20] conducted their study.

By using control data dating back to 2017 to establish trends and weekly case counts expressed as z -scores (a standardized measure equivalent to the number of standard deviations a given week's case numbers are from the overall study period mean), Bojti et al. demonstrated that ischemic stroke admissions, intravenous thrombolysis cases, and endovascular therapy cases experienced a significant negative deviation during the first and second COVID-19 waves in Hungary [20]. However, the ratio of both intravenous thrombolysis administrations to ischemic stroke admissions and endovascular interventions to ischemic stroke admissions actually significantly increased during both of Hungary's COVID-19 waves, suggesting that the decline in ischemic stroke admissions was disproportionately greater than the decline in acute revascularization therapies. Essentially, the number of acute stroke admissions during each COVID-19 wave decreased but the proportion of these admissions warranting emergent intravenous thrombolysis or endovascular intervention was greater for both COVID-19 waves. Furthermore, it appeared that the weekly number of COVID-19 cases might be related to the weekly number of stroke cases. Taking both COVID-19 waves into account, ischemic stroke admissions and acute revascularization interventions were inversely correlated to the weekly number of both new and cumulative cases of COVID-19. However, the overall significance of these inverse correlations appeared to be largely driven by the COVID-19 case counts of the second wave; a disproportionately greater suppression in acute stroke admissions and interventions appeared to occur relative to the much smaller number of COVID-19 cases yet more stringent public health mandated restrictions of the first wave.

Analysis of changes in ischemic stroke care at two distinct institutions in the USA

Inspired by the analysis from Bojti et al. [20], we examined if similar situations occurred at two

distinct medical institutions in the USA: Northwestern Memorial Hospital Comprehensive Stroke Center, Chicago, IL, and Oklahoma City Veterans Affairs Medical Center, Oklahoma City, OK. For the first institution, raw data was converted to standardized z -scores to compare across periods, as done by Bojti et al. We considered z -scores of magnitude 2 or greater to represent statistically significant deviations in case numbers at a given time point relative to the entire time period of comparison. For the second institution, we used the Mann–Kendall test for monotonic trend, with significance set at 0.05. All statistical analyses were performed using R version 4.03 (R Foundation for Statistical Computing, Vienna, Austria).

At the first institution, we examined the trends in acute “telestroke” consultations (audio/video evaluation provided by a stroke specialist for an acute stroke patient presenting to a remote emergency department) provided by the Northwestern Memorial Hospital Comprehensive Stroke Center during the months preceding the pandemic through April 2021 (Fig. 1). Northwestern Memorial Hospital provides ischemic stroke tele-consultation (telestroke) to a network of hospitals near the Chicago metropolitan area in Northern Illinois and Northwest Indiana, USA. For our analysis, we used data beginning in November 2019, since our telestroke hospital network membership has been unchanged since that time. We found that telestroke consultations were significantly depressed in April 2020 (z -score < -2), which was early in the first COVID-19 wave and the month of most severe public health restrictions in the Chicago area (stay-at-home order placed, complete closure of schools and all non-essential businesses). There also appeared to be a second, less drastic period of reduced telestroke consultation corresponding to the second COVID-19 wave and public health restrictions in Chicago with a z -score approaching -1 (no indoor dining and non-essential businesses open but with reduced capacity). During this second period, the reduction in telestroke consultation appeared to mirror the increase in the weekly rolling average daily COVID-19 case count but was not as depressed as during the severe public health restrictions of the first wave. Interestingly, the pattern of telestroke consultation seen at Northwestern Memorial Hospital during two waves of COVID-19 appears to be analogous to the pattern of ischemic stroke admissions described

by Bojti et al. in Hungary; in both locations, the magnitude of depression in stroke presentations appeared to correspond more to the severity of public health restrictions than the absolute number of COVID-19 cases during a wave.

At the second institution, we examined if the number of admissions for acute ischemic stroke and neurorehabilitation changed during the pandemic waves by comparing monthly data from January 1, 2019, to April 30, 2021, by using the Mann–Kendall test for monotonic trend. The Oklahoma City Veterans Affairs Medical Center (VAMC), Oklahoma City, OK, has a comprehensive stroke program providing acute inpatient care and outpatient follow-up for all veterans with stroke in the state of Oklahoma. This VAMC concurrently offers a unique neurorehabilitation program that also provides inpatient rehabilitation care for veterans with ischemic stroke after the initial acute phase of injury. Both the inpatient stroke and neurorehabilitation programs accept patients from direct referrals for admission originating in the emergency room and also as hospital transfers from any other medical facility in the state. In contrast to data from Bojti et al. from Hungary or from the Northwestern Memorial Hospital Comprehensive Stroke Center, no differences were observed for monthly admissions during the entire period studied, including the first or second COVID-19 waves, for acute stroke ($p=0.249$, average monthly admissions=19.3, range 17–21), neurorehabilitation ($p=0.521$, average monthly admissions=6.7, range 6–8), or combined stroke and neurorehabilitation admissions ($p=0.323$). During the first COVID-19 wave, severe public health restrictions were also in place in Oklahoma City (stay-at-home order placed, complete closure of schools and all non-essential businesses) between March 25 and April 24, 2020. During the second COVID-19 wave (November 2020/January 2021), the city maintained mandatory masking ordinance for indoor public spaces with additional guidelines on reduced capacity.

Discussion

What could be the reason underlying this decrease in ischemic stroke admissions and telestroke consultations during the first and second COVID-19 waves? Why did the effect on stroke care appear to be relatively less during the second COVID-19 wave despite a much greater number of COVID-19 cases?

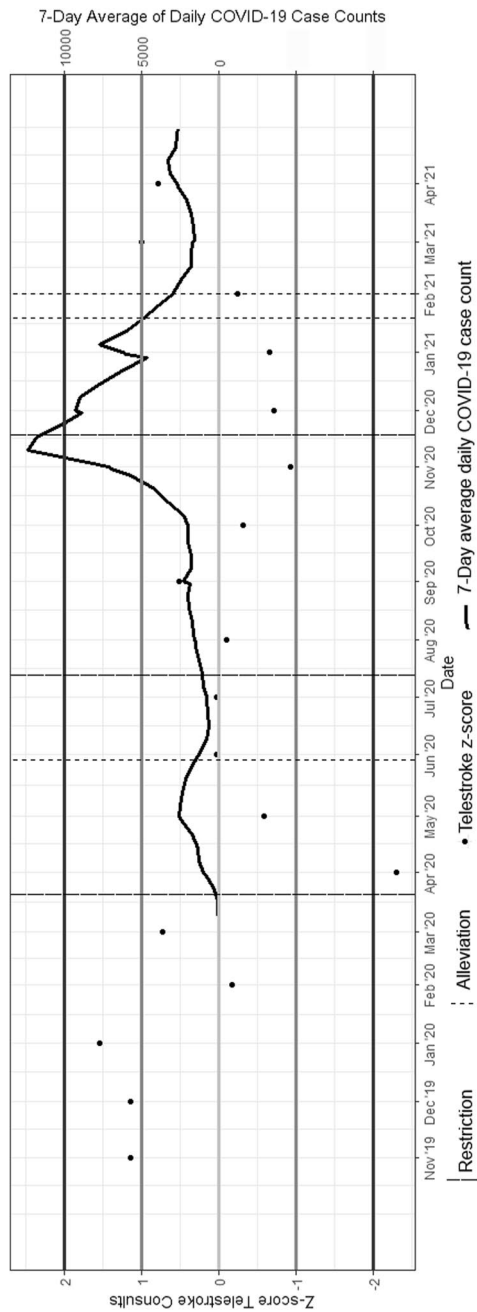


Fig. 1 Monthly z-scores (dots) of Northwestern Memorial Hospital Telestroke Network consults before and during the pandemic with the 7-day rolling average of daily COVID-19 case counts (bold curve) in Cook County, Illinois (source: Johns Hopkins Coronavirus Resource Center, <https://coronavirus.jhu.edu/data>). The major public health mandated restrictions (March/April 2020 stay-at-home order, all schools and non-essential business closed; July 2020 reduced non-essential business capacity; November 2020 indoor dining closed and reduced non-essential business capacity) and alleviations (May 29, 2020, stay-at-home order expires and non-essential businesses reopen at reduced capacity; January 19–25, 2021, less stringent Tier 2 and then Tier 1 mitigation restrictions go in to effect; February 2021 initial reopening phase begins) affecting Cook County, Illinois, are indicated

And what are the public health ramifications for the current pandemic and lessons that might be learned in responding to future disease outbreaks? SARS-CoV-2 is known to infect the vasculature promoting pro-inflammatory, pro-coagulation, and pro-fragility phenotypic changes in the cerebral vasculature, which promote the development of both intracranial hemorrhages and ischemic strokes. Therefore, a protective effect of the SARS-CoV-2 virus itself against stroke admission seems very unlikely. Could the stay-at-home lifestyle and home cooking and baking fads of the pandemic stay-at-home periods be responsible? This seems unlikely in light of studies showing that individuals became more sedentary and gained weight during stay-at-home periods [21, 22]. The control data from Bojti et al. provides unique support for an additional reasonable hypothesis: patients made a choice, based on emotional factors, not to seek medical attention unless symptoms were so severe that they perceived no other option. From 2017 through 2020, there were only three times when both weekly ischemic stroke admissions and the ratio of admissions to revascularization interventions in Hungary reached pandemic era *z*-score magnitudes greater than 3: the holiday weeks encompassing the Christmas and New Year's festivals of 2017, 2018, and 2019. One might hypothesize that during the emotionally joyful time of the high holiday season (and data from Bojti et al. also suggests to a lesser extent during the emotionally pleasant summer holiday season) patients may not seek medical attention for acute, yet more minor, stroke symptoms unless they perceive those symptoms to leave no choice but to interrupt their holiday festivities. After all, who would want to disrupt their holiday plans for "minor" symptoms? A holiday effect of hesitancy to seek medical care has previously been supported in the literature [23, 24]. In fact, an analysis of 25 years of data from the USA showed that rates of emergency room deaths and dead-on-arrival presentations to emergency rooms consistently spike on Christmas and New Year's day and no other days of the year [25], supporting a hypothesis that many patients choose to avoid/delay medical care at the holiday season at all costs. The COVID-19 pandemic was shown to exert multifaceted effects on mental health. COVID-19-related stress and anxiety can be related to the possibility of contracting and/or dying from the disease, actually having the disease, fear of family

members contracting the disease, fear of unknowingly infecting others, including family members, and/or experiencing significant financial burden due to the consequences of the pandemic, including job loss. Is it possible that separate and apparently opposite emotions of joy and happiness dictate patient behavior during the holidays while complex and negative emotions of fear due to incorrect perception of risk dictate behavior during pandemic lockdowns? Such a hypothesis would be consistent with the observation that the second COVID-19 wave in both Hungary and Chicago required many more active COVID-19 cases to precipitate an impact on ischemic stroke presentations similar to the first wave. Alternatively, improved public health messaging during the second wave from national and international organizations such as the American Heart Association and World Stroke Organization's "Stroke: Don't Stay At Home" campaign may have influenced patient behaviors as well. As patients learned what to expect from the first wave of COVID-19, perhaps it took many more daily COVID-19 cases to illicit similar or greater levels of fear to motivate their behaviors to avoid going to the hospital. What may be the ramifications of choosing not to seek medical care for "minor" symptoms during the holidays or the COVID-19 pandemic, regardless of the emotional motivation? Patients with ischemic stroke who do not seek medical attention are not likely to receive therapies that reduce their risk for future recurrent vascular events. These untreated "missed" strokes may translate to trends for greater morbidity and mortality through a higher occurrence of future strokes that may have otherwise been avoidable.

So what accounts for the differences seen between the two US systems of ischemic stroke care and in comparison to findings in Hungary? In our opinion, potential explanations for this difference may be linked to (1) regional differences in healthcare delivery in the USA as compared to a more centralized system in Hungary, (2) differences in patient characteristics and vascular risk (with older age, male gender and multiple vascular risk factors more prevalent in veterans [26, 27]), (3) a lower financial burden for veterans in terms of inpatient care and medication costs, (4) the unique position of the inpatient neurorehabilitation program as the sole facility providing this option for the entire population of veterans in the state of Oklahoma, (5) transient increase in medical

staff and admission capacity available by using federal resources, and (6) more heterogeneous perceptions of the risk of SARS-CoV-2 infection between residents of the densely populated Chicago area and the less densely populated Oklahoma City area compared to perceptions in Hungary. (7) Furthermore, the tertiary referral nature of the VAMC in the rural state of Oklahoma may more closely resemble a “mother-ship” paradigm of stroke care (direct admission to a comprehensive stroke center) than the strong spoke-and-hub model (also called drip-and-ship) of stroke care in Chicago. In fact, a meta-analysis suggested that stroke admission rates during the COVID-19 pandemic declined significantly for spoke-and-hub models but did not achieve a similar significant decline in “mother-ship” models [28]. In addition, the VAMC was able to rapidly increase inpatient staffing and inpatient bed capacity (both for intensive care unit and medical wards) during each COVID-19 wave using national coordination mechanisms in place for medical emergency situations, allowing for resources to be shifted between geographic regions and government agencies (including Department of Defense) at times of need. Many other factors such as socioeconomic status, ethnicity, and sex/gender may all also contribute to the differences observed in admissions in ischemic stroke systems of care during the various pandemic waves. The differences in sex/gender are particularly pronounced given the predominant male patient population of the VAMC relative to NMHC and across Hungary. Coping with the pandemic requires mental resilience, which exerts mitigating effects on generalized anxiety and depression. It is likely that differences in resilience of the contrasting patient populations determine their attitudes toward seeking medical help when they are under stress. It is possible that veterans’ attitudes are shaped by military culture, and the resilience of this patient group is greater than that of the general population. Attitudes toward the pandemic may also vary regionally, and though vaccination was not available during the periods evaluated, present-day differences in vaccination rates across Oklahoma (53%), Illinois (67%), and Hungary (63%) may provide some insight into differences in attitude toward the COVID-19 pandemic and the risks of SARS-CoV-2 [29]. Geographic and population density differences may also account for differences observed. With an average population of greater than 1.7 million, the City of Budapest is

closer in size to the City of Chicago (2.6 million) vs. Oklahoma City (600 K). Both Budapest and Chicago are similar in area as well, 202 square miles vs 234 square miles (525 km² vs 607 km²). Contrary to both of these cities, Oklahoma City occupies a much larger geographic area, 620 square miles in size (1607 km²).

Given the inherent differences in ischemic and hemorrhagic stroke presentation and treatment, our study focused only on ischemic stroke to assess the hypothesis presented by Bojti et al. in Hungary. Interestingly, larger studies across the USA utilizing Medicare claims data have recently demonstrated the differences in acute ischemic stroke and hemorrhagic stroke presentations during different time periods across the COVID-19 pandemic as well. Interestingly, the impact on hemorrhagic stroke presentation was far less than ischemic stroke presentation. Yang et al. [30] demonstrated dramatic reductions in acute ischemic stroke hospitalization across the USA during the initial wave of the pandemic, with significantly varying rates by state. Though hemorrhagic stroke makes up the minority of all stroke, it is generally more severe than ischemic stroke, and this difference in severity and incidence may partly explain the lesser impact of COVID-19 restrictions on hemorrhagic stroke hospitalizations. This hypothesis is also consistent with the observation made by Bojti et al., reporting a shift to more severe ischemic stroke cases admitted during the first and second waves of COVID-19.

It is not difficult to imagine that COVID-19 has had public health implications beyond the direct effects of the SARS-CoV-2 virus and that the fear of COVID-19 may have contributed to other important health issues going unaddressed. As health care systems stabilize after the waves of COVID-19, it will be important to attempt to mitigate the consequences of population behaviors leading to delay or avoidance of health care interactions for months on end. The cases of “missed” stroke that occurred during the pandemic waves should attempt to be identified so that appropriate therapies can be implemented to reduce the risk of future morbidity. While attempting to stem future infectious disease outbreaks, public health policy makers must appreciate how their infection control mandates affect the multiple facets of public health and how missed treatment opportunities for morbid diseases like stroke can result in collateral damage. Different patterns of health care delivery within each

country and across the world may provide valuable lessons to maximize all available resources for all the patients needing care. Reducing fear and uncertainty in the population through transparency and ensuring confidence in the adequate preparation, staffing, and provisioning of health care institutions may reduce fear-driven behaviors that undermine overall public health during times of public health emergency. Perhaps it remains true that the only thing we have to fear is fear itself when deciding to seek acute stroke care, no matter how minor or severe the symptoms may be.

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Declarations

Competing interests Dr. Calin Prodan, Dr. Ayush Batra, and Dr. Eric M. Liotta serve as Associate Editors for GeroScience. Dr. Zoltan Ungvari serves as Editor-in-Chief for GeroScience. The authors declare no competing financial interests.

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