

RAPID CLINICAL COMMUNICATION | OPEN ACCESS

Where are the missing stroke patients from the COVID-19 pandemic and what are their outcomes?

Renyu Liu¹, Anthony G Rudd², Jing Zhao³

The novel coronavirus disease 19 (COVID-19) can attack the central nervous system, (Ellul et al., 2020; Mao et al., 2020) and increase the likelihood of poor outcomes, including mortality for stroke patients (Yamakawa et al., 2020). The delivery of care to stroke patients is also significantly affected by COVID-19 (Liu et al., 2020; Markus and Brainin, 2020). A significant drop in stroke patient presentation to both outpatient clinics and admission to hospital during the COVID-19 pandemic has been reported across the world (Kansagra et al., 2020; Katsanos et al., 2020; Liu et al., 2020; Zhao et al., 2020c; Zhao et al., 2020a). The drop in hospital admissions results in a lower number of patients receiving thrombectomy and intravenous thrombolysis. Using a national data registry in combination with a national survey, we found that stroke admissions decreased about 38% across China and as a consequence, the numbers of cases of patients for thrombolysis as well as thrombectomy dropped by around 25% respectively (Zhao et al., 2020c). An international survey demonstrated that in the countries participating, the number of stroke admissions dropped about 42% (Liu et al., 2020). We have been proposing vigorous education programs to encourage stroke patients to come to hospitals for immediate care (Zhao and Liu, 2017; Zhao et al., 2018; Zhao et al., 2020c; Zhao et al., 2020a). It is critical to educate the public that stroke is such a devastating disease often causing death or lifelong profound disability. Many hospitals and clinics have adopted telemedicine to help patients to access proper stroke care in the middle of shutdown or partial shutdown of the outpatient clinics across the world (Zhao et al., 2020b). The sharp drop in stroke admissions is likely to be for one of two reasons: a decrease in the proportion of stroke patients who failed to present for medical attention or a reduction in the incidence of stroke in the population. Recent studies have indicated that COVID-19 can induce stroke and the coexistence of COVID-19 often results in much more severe syndrome with a worse outcome (Ntaios et al., 2020). It seems unlikely that somehow COVID-19 caused a reduction in incidence, but it is possible that risk factors changed during quarantine periods possibly with less stress,

less exposure to air pollution, or reduced risky behavior such as smoking and alcohol consumption. Our study indicated that the drop in stroke admissions was mainly caused by the unwillingness of the stroke patient to come to the hospital, in part due to poor awareness of the potential severity of stroke and fear of contracting COVID-19 from staff and other patients (Zhao et al., 2020c). Even if the incidence of stroke remained the same, the sharp drop in stroke patient admissions means many stroke patients did not receive proper medical care including thrombolysis and thrombectomy. So, the questions are what has happened to the missing patients and what has the impact been on their outcomes?

There are two major types of strokes: hemorrhagic stroke and ischemic stroke, with around 80-90% being ischemic in the US and Europe and 60-70% in China (Writing Group et al., 2016). Hemorrhagic strokes may require emergency surgery. Patients presenting with hemorrhage often have headache combined with focal neurological deficits and because of the pain tend to present more promptly to the clinic than ischemic stroke patients, who are usually pain free. The drop in stroke admissions was mainly for ischemic strokes. The signs and symptoms of ischemic stroke vary widely, especially for those who have only mild or moderate stroke, making them potentially difficult to be recognized in a timely manner. Some of the signs of stroke can only be recognized or noticed by person nearby rather than the patient themselves. During the pandemic, because of self-quarantine and social distancing, recognition by third parties may have been reduced contributing to the delay or absence of hospital presentation. Even if some mild symptoms or signs were recognized by somebody, the patient may have been less willing to call the emergency phone numbers (911 in the US and Canada, 999 in England, 112 in most of the European countries and 120 in China) and to be sent to the hospital to be evaluated for potential stroke. A recent report indicated that the drop in stroke admissions was mainly for mild or moderate strokes (Diegoli et al., 2020). These mild and moderate strokes could potentially recover spontaneously, however we know that

¹Department of Anesthesiology and Critical Care, Perelman School of Medicine at the University of Pennsylvania, Philadelphia PA, USA. ²Stroke Medicine, Kings College London, England. ³Department of Neurology, Minhang Hospital, Fudan University, Shanghai, China.

Correspondence should be addressed to Renyu Liu (RenYu.Liu@penmedicine.upenn.edu).

the natural history of stroke is often one where there are mild precursor symptoms that then deteriorate into severe symptoms without correct treatment. Transient ischemic attack (TIA) is a very mild form of stroke that completely resolves within 24 hours but usually within just a few minutes. But again, the risk of a completed stroke after TIA is high with up to a third presenting with stroke in the month after the TIA. With proper diagnosis and prevention treatments this rate can be dramatically reduced. Therefore, proper preventive strategies should be in place to avoid such tragedies.

There is little doubt that the reduction in stroke admissions and consequently effective prevention and treatment means that there are patients who have died unnecessarily or survived with preventable disability. If this is correct we might expect to see an increase in demand for rehabilitation both as in-patients and in clinics where such facilities are available and affordable for the patients. Based on our personal communication, a significant increase in rehabilitation evaluations in such clinics has been observed. Unfortunately, there are likely too many patients in both high, middle, and low income countries who will have had neither adequate acute care nor any rehabilitation, and will therefore have their lives and those of their close family blighted. Therefore, well-designed studies are needed to confirm our hypothesis and mitigate the prolonged impact of COVID-19 on stroke care.

References

- Diegoli H, Magalhaes PSC, Martins SCO, Moro CHC, Franca PHC, Safanelli J, Nagel V, Venancio VG, Liberato RB, Longo AL (2020) Decrease in hospital admissions for transient ischemic attack, mild, and moderate stroke during the COVID-19 era. *Stroke* 51:2315-2321.
- Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, Kneen R, Defres S, Sejvar J, Solomon T (2020) Neurological associations of COVID-19. *The Lancet Neuro* 19:767-783.
- Kansagra AP, Goyal MS, Hamilton S, Albers GW (2020) Collateral effect of Covid-19 on stroke evaluation in the United States. *NEJM* 383:400-401.
- Katsanos AH, de Sa Boasquevisque D, Ahmed Al-Qami M, Shawawrah M, McNicoll-Whiteman R, Gould L, Van Adel B, Sahlas DJ, Ng KKH, Perera K, Sharma M, Oczkowski W, Pikula A, Shoamanesh A, Catanese L (2020) In-hospital delays for acute stroke treatment delivery during the COVID-19 pandemic. *Can J Neurol Sci*:1-17.
- Liu R, Zhao J, Fisher M (2020) The global impact of COVID-19 on acute stroke care. *CNS Neurosci Ther*.
- Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, Chang J, Hong C, Zhou Y, Wang D, Miao X, Li Y, Hu B (2020) Neurologic manifestations of hospitalized patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neuro* 77:683-690.
- Markus HS, Brainin M (2020) COVID-19 and stroke-A global World Stroke Organization perspective. *Int J Stroke* 15:361-364.
- Ntaios G et al. (2020) Characteristics and Outcomes in Patients With COVID-19 and Acute Ischemic Stroke: The Global COVID-19 Stroke Registry. *Stroke* 51:e254-e258.
- Writing Group M et al. (2016) Heart disease and stroke statistics-2016 update: A report from the American Heart Association. *Circulation* 133:e38-360.
- Yamakawa M, Kuno T, Mikami T, Takagi H, Gronseth G (2020) Clinical characteristics of stroke with COVID-19: A systematic review and meta-analysis. *J Stroke Cerebrovasc Dis* 29:105288.
- Zhao J, Liu R (2017) Stroke 1-2-0: a rapid response programme for stroke in China. *Lancet Neurol* 16:27-28.
- Zhao J, Rudd A, Liu R (2020a) Challenges and potential solutions of stroke care during the coronavirus disease 2019 (COVID-19) outbreak. *Stroke* 51:1356-1357.
- Zhao J, Fisher M, Liu R (2020b) Slower recovery of outpatient clinics than inpatient services for stroke and other neurological diseases after COVID-19 Pandemic. *CNS Neurosci Ther* doi: 10.1111/cns.13459.
- Zhao J, Eckenhoff MF, Sun WZ, Liu R (2018) Stroke 112: A universal stroke awareness program to reduce language and response barriers. *Stroke* 49:1766-1769.
- Zhao J, Li H, Kung D, Fisher M, Shen Y, Liu R (2020c) Impact of the COVID-19 Epidemic on Stroke Care and Potential Solutions. *Stroke* 51:1996-2001.