BRIEF REPORT

Delays in Stroke Onset to Hospital Arrival Time During COVID-19

Kay-Cheong Teo, MBBS, FHKAM; William C.Y. Leung, MBBS; Yuen-Kwun Wong, MSc; Roxanna K.C. Liu, MPH; Anna H.Y. Chan, MPhil; Olivia M.Y. Choi, MPsych; Wing-Man Kwok, MBBS; Kung-Ki Leung, RN; Man-Yu Tse, MBBS, FHKAM; Raymond T.F. Cheung, MD, PhD; Anderson Chun-On Tsang[®], MBBS, FRCS; Kui Kai Lau[®], DPhil

BACKGROUND AND PURPOSE: The current coronavirus disease 2019 (COVID-19) pandemic represents a global public health crisis, disrupting emergency healthcare services. We determined whether COVID-19 has resulted in delays in stroke presentation and affected the delivery of acute stroke services in a comprehensive stroke center in Hong Kong.

METHODS: We retrospectively reviewed all patients with transient ischemic attack and stroke admitted via the acute stroke pathway of Queen Mary Hospital, Hong Kong, during the first 60 days since the first diagnosed COVID-19 case in Hong Kong (COVID-19: January 23, 2020–March 24, 2020). We compared the stroke onset to hospital arrival (onset-to-door) time and timings of inpatient stroke pathways with patients admitted during the same period in 2019 (pre–COVID-19: January 23, 2019–March 24, 2019).

RESULTS: Seventy-three patients in COVID-19 were compared with 89 patients in pre–COVID-19. There were no significant differences in age, sex, vascular risk factors, nor stroke severity between the 2 groups (P>0.05). The median stroke onset-to-door time was ≈1-hour longer in COVID-19 compared with pre–COVID-19 (154 versus 95 minutes, P=0.12), and the proportion of individuals with onset-to-door time within 4.5 hours was significantly lower (55% versus 72%, P=0.024). Significantly fewer cases of transient ischemic attack presented to the hospital during COVID-19 (4% versus 16%, P=0.016), despite no increase in referrals to the transient ischemic attack clinic. Inpatient stroke pathways and treatment time metrics nevertheless did not differ between the 2 groups (P>0.05 for all comparisons).

CONCLUSIONS: During the early containment phase of COVID-19, we noted a prolongation in stroke onset to hospital arrival time and a significant reduction in individuals arriving at the hospital within 4.5 hours and presenting with transient ischemic attack. Public education about stroke should continue to be reinforced during the COVID-19 pandemic.

Key Words: coronavirus disease = public health = stroke

Stroke is a devastating disease with high mortality and morbidity rates. The timely and effective delivery of acute stroke care, especially reperfusion therapy for ischemic stroke, significantly improves stroke outcomes.^{1,2} The provision of acute stroke care has been put to the test during the coronavirus disease 2019 (COVID-19) outbreak. Since its emergence in December 2019 in China, it has rapidly evolved into a global pandemic crippling healthcare services around the world. Hong Kong (HK) recorded its first COVID-19 case on January 23, 2020, and is still in its containment phase as of the current writing, without sustained community spread. Nonemergency services throughout hospitals in HK have been adjusted to cope with the outbreak, and workforce allocation for acute stroke pathways has been maintained as much as possible.

Nevertheless, it remains uncertain whether COVID-19 has influenced public behavior in seeking medical

For Sources of Funding and Disclosures, see page xxx.

© 2020 American Heart Association, Inc.

Correspondence to: Kui Kai Lau, DPhil, Division of Neurology, Department of Medicine, Queen Mary Hospital, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, Email gkklau@hku.hk or Anderson Chun-On Tsang, MBBS, FRCS, Division of Neurosurgery, Department of Surgery, Queen Mary Hospital, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, Email acotsang@hku.hk

Stroke is available at www.ahajournals.org/journal/str

Nonstandard Abbreviations and Acronyms

COVID-19	coronavirus disease 2019		
HK	Hong Kong		
TIA	transient ischemic attack		
IV r-tPA	intravenous recombinant tissue-type plasminogen activator		

attention for stroke and whether stroke services have been affected. We, therefore, compared the stroke onset to hospital arrival (onset-to-door) time and timings of inpatient stroke pathways during the COVID-19 outbreak with a similar period in 2019.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request. We retrospectively reviewed consecutive patients with transient ischemic attack (TIA)/stroke who were admitted to Queen Mary Hospital, HK, via the acute stroke pathway during the first 60 days since the first diagnosed case of COVID-19 in HK (COVID-19: January 23, 2020–March 24, 2020). We compared these patients with those admitted during the same period in 2019 (pre–COVID-19: January 23, 2019–March 24, 2019). Patients were retrieved from the ongoing Queen Mary Hospital stroke registry, which is approved by the local research ethics board.

Queen Mary Hospital is a comprehensive stroke center in HK that admits ≈800 patients with TIA/stroke every year. Our acute stroke pathway encompasses a multidisciplinary team that enrolls patients with stroke presenting to the A&E Department within 24 hours of symptom onset or last seen well time. The diagnosis of TIA/stroke was confirmed by the attending neurologist or neurosurgeon. We excluded patients who did not have a TIA/stroke or were admitted to Queen Mary Hospital without going through the acute stroke pathway, such as patients presenting >24 hours after symptoms onset.

We collected details of baseline demographics, vascular risk factors, stroke subtype and severity, and details of acute stroke treatment of patients during the COVID-19 and pre-COVID-19 periods. Stroke onset-to-door time was defined as the duration between symptoms onset or last seen well time to A&E Department arrival; door-to-needle time was the duration between A&E Department arrival to the administration of IV r-tPA (intravenous recombinant tissue-type plasminogen activator), whereas door-to-groin time was the time between A&E Department arrival to groin puncture for endovascular thrombectomy.

Baseline demographics, vascular risk factors, stroke subtypes and severity, stroke onset-to-door time, and critical time points in inpatient acute stroke care between COVID-19 versus pre-COVID-19 were compared using *t* test, χ^2 , and Mann-Whitney *U* test where appropriate. All analyses were done with Stata version 14, and a *P* value of <0.05 was considered statistically significant.



Figure 1. Cumulative number of coronavirus disease 2019 (COVID-19) cases in Hong Kong during January 23, 2020–March 24, 2020.

RESULTS

During the period January 23, 2020 to March 24, 2020, a total of 386 COVID-19 cases were diagnosed in HK (Figure 1). Seventy-three and 89 patients with TIA/ stroke were admitted through the acute stroke pathway during the COVID-19 and pre-COVID-19 periods, respectively. No significant differences in age, sex, vascular risk factors, nor stroke severity were noted between the 2 groups (Table). There were fewer patients admitted with a TIA during COVID-19 (3/73 [4.1%] versus 14/89 [15.7%], P=0.016), despite no significant increase in referrals to the TIA clinic (P>0.05).

The median stroke onset-to-door arrival time during COVID-19 was \approx 60 minutes longer compared with pre-COVID-19 (154 [60–618] minutes versus 95 [58–291], P=0.12), and there was a significantly lower proportion of individuals with onset-to-door time within 4.5 hours (40/73 [54.8%] versus 64/89 [71.9%], P=0.024; Figure 2). There were otherwise no significant differences in the ambulance scene arrival to hospital arrival time, proportion of patients receiving reperfusion therapy, door-to-needle time, and mechanical thrombectomy procedural times during the 2 periods (Table).

DISCUSSION

Our results highlight the possible increased reluctance of patients in seeking hospital treatment for TIA/stroke symptoms during the COVID-19 outbreak. Compared with the same period in 2019, during COVID-19, the median symptom onset-to-door time was up to 60 minutes longer, fewer patients with TIA sought hospital treatment, and the proportion of patients arriving within the therapeutic time window of IV r-tPA was significantly lower.

Delays in seeking care or not seeking care would be detrimental to stroke outcome. Time is brain, and earlier reperfusion for ischemic stroke is associated with

Table.	Clinical Characteristics, Stroke Classification and			
Treatment of Pre-COVID-19 Versus COVID-19 Patients				

	Pre-COVID-19 (N=89)	COVID-19 (N=73)	<i>P</i> Value
Mean age, y (SD)	73.6 (13.1)	70.1 (16.2)	0.14
Males, %	45 (50.6)	32 (43.8)	0.39
Ever-smokers, %	16 (18.0)	19 (26.0)	0.22
Hypertension, %	60 (67.4)	47 (64.4)	0.69
Diabetes mellitus, %	23 (25.8)	16 (21.9)	0.56
Ischemic heart disease, %	10 (11.2)	8 (11.0)	0.96
Atrial fibrillation, %	13 (14.6)	13 (17.8)	0.58
Stroke classification and severity			
Transient ischemic attack, %	14 (15.7)	3 (4.1)	0.016
Ischemic stroke, %	52 (58.4)	47 (64.4)	0.44
Hemorrhagic stroke, %	23 (25.8)	23 (31.5)	0.43
Median baseline NIHSS (IQR)	6 (2–16)	7 (3–16)	0.76
Stroke treatment			
Median onset-to-door time, min (IQR)	95 (58–291)	154 (60–618)	0.12
Onset-to-door within 4.5 h, %	64 (71.9)	40 (54.8)	0.024
Median ambulance scene arrival to hospital arrival time, min (IQR)	24 (20–30)	26 (22–30)	0.31
Intravenous thrombolysis, %*	8 (15.4)	7 (14.9)	0.95
Median door-to-needle time, min (IQR)	67 (47–85)	53 (36–77)	0.25
Mechanical thrombectomy, %*	7 (13.4)	4 (8.5)	0.43
Median door-to-groin puncture time, min (IQR)	119 (104–132)	98 (63–106)	0.059
Median arrival to OT-to-reperfusion time, min (IQR)	88 (76–120)	82 (58–90)	0.39

COVID-19 indicates coronavirus disease 2019; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; and OT, operation theater. *Only include patients with ischemic stroke.

better clinical outcomes.³ Also, as the therapeutic time window for reperfusion therapy is narrow, any delays in seeking care would seriously jeopardize the eligibility for

treatment. Although we were unable to evaluate the actual number of patients with TIA who did not seek care during COVID-19, the lower number of TIAs going through the acute stroke pathway suggests many patients with TIA may not have sought medical attention. Not seeking care for TIA is potentially devastating, as around 10% to 20% of patients with TIA may subsequently develop a stroke within 90-days.^{4,5} Early treatment of TIA could reduce this risk by 80%.⁶ Hence, to ensure appropriate treatment could be provided to patients with TIA/stroke during COVID-19, public awareness campaigns on symptoms of TIA/stroke and the importance of seeking immediate medical care should be enhanced.

Our study is limited by its retrospective nature and inclusion of a small number of subjects managed in a single comprehensive stroke center based in HK. Although our results reflected patients' possible reluctance to attend hospitals, we were unable to confirm this with individual patients due to the retrospective nature of the study. Further studies focusing on the changes in patients' behavior during COVID-19 are warranted. As a hospital-based stroke registry, we were also not able to determine whether ambulance response times have changed during COVID-19. Nevertheless, this is indeed possible due to the need for enhanced disinfection procedures between patients (personal communication with ambulance services). Our study was also limited, as due to a small number of subjects, we were unable to determine whether stroke epidemiology has changed during COVID-19. A brief analysis on all patients with TIA/stroke admitted to our hospital (mainly including those presenting beyond 24 hours into the current study cohort) revealed that the proportion of ischemic (82/122 [67.2%] versus 94/152 [61.8%]) and hemorrhagic strokes (32/122 [26.2%] versus 38/152 [25.0%]; all P>0.05) appeared similar during COVID-19 and pre-COVID-19 periods. Further studies in larger



Figure 2. Comparison between (**A**) stroke onset-to-door time, door-to-needle time, and (**B**) proportion of patients with onset-to-door time within 4.5 h during pre-COVID-19 and COVID-19. COVID-19 indicates coronavirus disease 2019.

Although HK is still in the containment phase of managing COVID-19, the stroke service appears to have mostly maintained. However, in countries that are hard-hit by the outbreak, stroke centers have been reorganized to assist the fight against COVID-19,⁷ reflecting the impact of COVID-19 on stroke care. Globally, every effort is needed to ensure that acute stroke care is not compromised. As Zhao et al⁸ poignantly pointed out, centralized diversion to protected stroke centers that remain fully operational, and informing the public of such system is vital to prevent tragedies of potentially treatable patients with stroke being denied appropriate treatment during this pandemic.

ARTICLE INFORMATION

Received April 4, 2020; accepted May 1, 2020.

Affiliations

From the Division of Neurology, Department of Medicine (K.-C.T., W.C.Y.L., Y.-K.W., R.K.C.L., A.H.Y.C., K.-K.L., M.-Y.T., R.T.F.C., K.K.L.) and Division of Neurosurgery, Department of Surgery (O.N.Y.C., A.C.-O.T.), Queen Mary Hospital, LKS Faculty of Medicine, The University of Hong Kong. Department of Accident and Emergency, Queen Mary Hospital, Hong Kong (W.-M.K.).

Sources of Funding

The Hong Kong (HK) West Cluster Stroke Registry was supported by the Health and Medical Research Fund, HK Government Food & Health Bureau (Ref. 06172626).

Disclosures

K.K. Lau reports grants from Health and Medical Research Fund, Hong Kong Government Food and Health Bureau, and grants from Mr and Mrs Tam Wing

Fan Stroke and Dementia Research Fund during the conduct of the study, grants, personal fees, and nonfinancial support from Boehringer Ingelheim, grants from Sanofi, grants from Eisai, grants from Amgen, and grants and non-financial support from Pfizer outside the submitted work. The other authors report no conflicts.

REFERENCES

- Lees KR, Emberson J, Blackwell L, Bluhmki E, Davis SM, Donnan GA, et al; Stroke Thrombolysis Trialists' Collaborators Group. Effects of alteplase for acute stroke on the distribution of functional outcomes: a pooled analysis of 9 trials. *Stroke*. 2016;47:2373–2379. doi: 10.1161/STROKEAHA.116.013644
- Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al; HERMES Collaborators. Endovascular thrombectomy after largevessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
- Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a systematic review. JAMA. 2015;313:1451–1462. doi: 10.1001/jama.2015.3058
- Coull AJ, Lovett JK, Rothwell PM; Oxford Vascular Study. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. *BMJ*. 2004;328:326. doi: 10.1136/bmj.37991.635266.44
- Kleindorfer D, Panagos P, Pancioli A, Khoury J, Kissela B, Woo D, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. *Stroke*. 2005;36:720-723. doi: 10.1161/01. STR.0000158917.59233.b7
- Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JN, et al; Early Use of Existing Preventive Strategies for Stroke (EXPRESS) Study. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *Lancet.* 2007;370:1432–1442. doi: 10.1016/S0140-6736(07)61448-2
- 7. European Stroke Organization. Stroke Care During COVID-19 Pandemic. https://eso-stroke.org/eso/stroke-care-during-covid-19-pandemic/. March 16, 2020. Accessed April 3, 2020.
- Zhao J, Rudd A, Liu R. Challenges and potential solutions of stroke care during the coronavirus disease 2019 (COVID-19) outbreak. *Stroke*. 2020;51:1356–1357. doi: 10.1161/STROKEAHA.120.029701