Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Impact of Coronavirus Disease 2019 on Time Delay and Functional Outcome of Mechanical Thrombectomy in Tokyo, Japan

Masahiro Katsumata, a Takahiro Ota, b Junya Kaneko, c Hiroyuki Jimbo, d Rie Aoki, e Shigeta Fujitani, f Masahiko Ichijo, g Masato Inoue, h Keigo Shigeta, i Yoshifumi Miyauchi, j Yu Sakai, k Hideki Arakawa, l Yoshinobu Otsuka, m Kenichi Ariyada, n Yoshiaki Kuroshima, o Takahisa Fuse, p Yoshiaki Shioiwa, q and Teruyuki Hirano, r

Objectives: An association has been reported between delays in the onset-to-door (O2D) time for mechanical thrombectomy (MT) and outbreaks of coronavirus disease 2019 (COVID-19). However, the association between other MT time courses or functional outcomes and COVID-19 outbreaks remains unclear. We compared the time courses of stroke pathways or functional outcomes in 2020 (the COVID-19 era) with those in 2019 (the pre-COVID-19 era) in Tokyo, Japan. Materials and methods: This retrospective observational study used data from the Tokyo-tama-REgistry of Acute endovascular Thrombectomy (TREAT), a multicenter registry of MT for acute large vessel occlusion in the Tokyo Metropolitan Area. Patients who had undergone acute MT from January 2019 to December 2020 were included. Patients were classified by the year they had undergone MT (2019 or 2020). Results: In total, 477 patients were analyzed. O2D time was significantly longer in 2020 (146.0 min) than in 2019 (105.0 min; \( p = 0.034 \)). No significant difference in door-to-puncture time (D2P) time or modified Rankin Scale (mRS) score 0–2 at 90 days was seen between 2019 and 2020. In the subgroup analysis, O2D time was significantly longer in the first half of 2020 compared with 2019. Multivariable logistic regression analysis revealed that the year 2020 was a independent predictor of longer O2D time, but not for mRS score 0–2 at 90 days. Conclusions: Although O2D time was significantly longer in the COVID-19 compared with the pre-COVID-19 era, D2P may not be significantly delayed and functional outcomes may not be different, despite the COVID-19 pandemic.

From the "Department of Neurology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan; bDepartment of Neurosurgery, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan; cDepartment of Emergency and Critical Care Medicine, Nippon Medical School Tama Nagayama Hospital, Tokyo, Japan; dDepartment of Neurosurgery, Tokyo Medical University Hachioji Medical Center, Tokyo, Japan; eDepartment of Neurosurgery, Tokai University Hachioji Hospital, Tokyo, Japan; fDepartment of Endovascular Neurosurgery, Toranomon Hospital, Tokyo, Japan; gDepartment of Neurology, Musashino Red Cross Hospital, Tokyo, Japan; hDepartment of Neurosurgery, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan; iDepartment of Neurosurgery, National Hospital Organization Disaster Medical Center, Tokyo, Japan; jDepartment of Neurology, Showa University Koto Toyosu Hospital, Tokyo, Japan; kDepartment of Neurosurgery, Showa General Hospital, Tokyo, Japan; lDepartment of Neurosurgery, Omori Red Cross Hospital, Tokyo, Japan; mDepartment of Neurology, Machida Municipal Hospital, Tokyo, Japan; nDepartment of Neurosurgery, Tokyo Metropolitan Bokuto Hospital, Tokyo, Japan; oDepartment of Neurosurgery, Hino Municipal Hospital, Tokyo, Japan; pDepartment of Neurosurgery, Public Fussa Hospital, Tokyo, Japan; qDepartment of Neurosurgery, Kyorin University, Tokyo, Japan; and rDepartment of Stroke and Cerebrovascular Medicine, Kyorin University, Tokyo, Japan.

Received June 7, 2021; revision received August 4, 2021; accepted August 8, 2021.

Corresponding author. E-mail: ktmasahiro@gmail.com.

1052-3057/ - see front matter
© 2021 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.106051
Key Words: COVID-19—Acute ischemic stroke—Thrombectomy—Epidemiology

© 2021 Elsevier Inc. All rights reserved.

Introduction

Several papers from around the world have reported that outbreaks of coronavirus disease 2019 (COVID-19) have led to the following time delays associated with endovascular mechanical thrombectomy (MT) for patients with acute ischemic stroke (AIS): onset-to-door (O2D) time,1,2 door-to-puncture (D2P) time and door-to-recanalization time.3 Several speculative factors may explain these delays, such as a collapse of emergency services focused on patients with COVID-192 and patients’ fear of exposure to COVID-19 through interactions within the healthcare system.2,4

In Japan, the first patient with COVID-19 was reported on January 15, 2020. During 2020, waves of the COVID-19 pandemic may have led to time delays or changes in functional outcomes after MT. Previous reports have reported reduced numbers of patients admitted for stroke, thrombolysis, and thrombectomy worldwide5 and in Tokyo.6 However, whether the status of the COVID-19 pandemic in Japan is correlated with time delays to, or changes in functional outcomes after, MT remains poorly understood.

Therefore, this study aimed to compare the time courses of stroke pathways or functional outcomes in 2020 (the COVID-19 era) with those in 2019 (the pre-COVID-19 era) in Tokyo, Japan using data from the Tokyo-tama-REgistry of Acute endovascular Thrombectomy (TREAT) database.

Methods

Study design and oversight

This retrospective observational study used prospectively and retrospectively collected data from TREAT (UMIN-CTR: UMIN000026888), a multicenter registry of MT for acute large vessel occlusion (LVO) in the Tokyo Metropolitan Area.7 The survey covered patients with LVO who underwent acute MT between January 2019 and December 2020. The participating facilities were 18 thrombectomy-capable stroke centers in the Tokyo metropolis. The study protocol was approved by the ethics committee of each participating center. Written, informed consent was obtained from all participants or their legal representative.

Patient selection

The inclusion criteria for this study were: 1) underwent acute MT and 2) was directly transferred by emergency medical services (EMS) from home/scene or another hospital. The exclusion criteria were: 1) missing data about O2D, last-known-well (LKW), or D2P time, 2) missing data about modified Rankin Scale (mRS) scores at 90 days after MT, 3) pre-mRS score 3–5, and 4) O2D time over 24 h.

Procedure

The physician in charge of therapy in the facility determined the therapeutic approach deemed most appropriate. Recanalization status was classified using the modified Thrombolysis In Cerebral Infarction scale.8

Outcomes

The primary outcomes were O2D time, D2P time, and mRS score at 90 days. Symptomatic intracranial hemorrhage was defined as any intracranial hemorrhage related to worsening of the National Institutes of Health Stroke Scale (NIHSS) score ≥4 or requiring any additional procedure.

Statistical analysis

Analysis was performed using SPSS 26 software (IBM, Armonk, NY, USA) and R 4.1.0 for measurement of intraclass correlation (ICC) and fixed effect model. The baseline characteristics and outcomes between the cases in 2019 (pre-COVID-19 era) and 2020 (COVID-19 era) were compared using the Mann–Whitney U-test for continuous variables and the χ² test for categorical variables. The threshold for significance was p < 0.05. We estimated ICC to estimate the center effect and used fixed effect model for including center effect in each outcome (O2D, D2P and mRS at 90 days). We performed subgroup analysis by comparing baseline characteristics and outcomes between 2019 and 2020 every 3 months. Multivariable logistic regression analysis was conducted to assess independent predictors of O2D time with adjustments for years and previously identified potential predictors9,10 of mRS scores at 90 days with adjustments for years and previously identified potential predictors of mRS at 90 days.11–15 To deal with missing data, we used complete case analysis for continuous variables and categorized categorical variables as unknown.

Results

Fig. 1 shows the numbers of cases in Tokyo, Japan who tested positive for COVID-19, hospitalized patients, and cases who did not fulfill the Tokyo Rule which requires calls to over five institutions or taking over 20 min from the start of hospital selection to find an institution that could accept the patient; this indicates the difficulty of emergency transportations to hospital. The COVID-19 pandemic has been characterized by several waves and
peaks. In the peak of the first wave, from April 7 to May 31, 2020, the Japanese government declared a state of emergency and asked people to self-quarantine. Among 693 patients who met the inclusion criteria between January 2019 and December 2020, 477 were included in the present study (Fig. 2). The patients’ baseline and procedural characteristics are shown in Table 1.

NIHSS scores were significantly higher in 2020. Diagnostic modalities for occluded vessels and stroke etiologies significantly differed between 2019 and 2020. The outcomes are summarized in Tables 2 and 3. O2D time was significantly longer in 2020 (146.0 min) than in 2019 (105.0 min; \( p = 0.034 \)). Although O2D time or LKW time to EMS call time and arrival at the site to departure time did not significantly differ between 2019 and 2020, EMS call to arrival at the site (2019 vs. 2020; 8.0 vs. 9.0 min, \( p = 0.005 \)), door (H1: hospital transferred to first) to departure (H1) time (95.0 vs. 113.5 min, \( p = 0.008 \)), and door (H1) to door (H2: hospital transferred to secondarily for thrombectomy) time (112.0 vs. 133.0 min, \( p = 0.008 \)) were all significantly longer in 2020 than in 2019. Although not significantly different, O2D or LKW to EMS call was longer in 2020 than in 2019. No significant differences were seen in D2P time, mRS score 0–2 at 90 days, or other secondary outcomes between 2019 and 2020. The ICC of each outcome was 0.0169 (O2D), 0.232 (D2P), and 0.0354 (mRS at 90 days); large ICC was measured in D2P. The fixed effect model to include the center effect revealed that the coefficients (± standard error: SE) of year and O2D, D2P, and mRS at 90 days were 0.22 ± 0.093 (\( p = 0.0183 \)), 0.018 ± 0.051 (\( p = 0.718 \)), and -0.34 ± 0.19 (\( p = 0.0738 \)).

A summary of the subgroup analysis is shown in Table 4. Compared with 2019, O2D time was significantly longer from January to March 2020, the beginning of the COVID-19 pandemic in Tokyo (2019 vs. 2020; 84.5 vs. 140.0 min, \( p = 0.025 \)), and from April to June 2020, the
peak of the first wave (2019 vs. 2020; 105.0 vs. 155.0 min, \( p = 0.025 \)). In addition, D2P time was significantly longer from October to December 2020, the peak of the third wave (2019 vs. 2020; 62.5 vs. 82.0 min, \( p = 0.022 \)). No significant difference in mRS score at 90 days was found between 2019 and 2020. Since the median time of O2D in total patients was 140.0 min, patients whose O2D > 140.0 were classified in longer O2D time group. The results of the multivariable logistic regression analysis of O2D time (Table 5) revealed that LKW time, transferred from another hospital, lower NIHSS score, and year 2020 (odds ratio [OR]: 1.72; 95% confidence interval [CI]: 1.06–2.82; \( p = 0.028 \)) were independent predictors of a longer O2D time. The results of the multivariable logistic regression analysis of mRS score 0–2 at 90 days revealed that year was not associated with mRS score 0–2 at 90 days (Table 6).

### Discussion

The results of this study revealed that O2D time was significantly longer in 2020 than in 2019, but not D2P time or mRS score at 90 days. In the subgroup analysis, O2D time was also significantly longer in the first half of 2020 than in 2019, and D2P time was significantly longer from October to December 2020 than in 2019. According to the multivariable logistic regression analysis, year 2020 was an independent predictor of a longer O2D time; however, it was not associated with mRS 0–2 at 90 days. Previous studies have reported that COVID-19 outbreaks were associated with delays in O2D time.1,2 The breakdown in emergency services caused by COVID-19 outbreaks and patients’ fears of exposure to the disease may be speculative factors explaining the time delays during the COVID-19 era.2 Another study reported that factors such as a

---

**Table 1. Patients’ baseline characteristics.**

|                          | 2019 (n = 242) | 2020 (n = 235) | \( p \) |
|--------------------------|---------------|---------------|-------|
| Age median (IQR)         | 76.0 (70.0–82.0) | 77.0 (68.0–83.0) | 0.734 |
| Gender/Male              | 156 (64.5%) | 135 (57.4%) | 0.116 |
| LKW                      | 101 (41.7%) | 116 (49.4%) | 0.094 |
| Previous mRS score       |               |               |       |
| 0                        | 195 (80.6%) | 168 (71.5%) | 0.067 |
| 1                        | 26 (10.7%)  | 37 (15.7%)  |       |
| 2                        | 21 (8.7%)   | 30 (12.8%)  |       |
| Transferred from another hospital | | | |
| History                  |               |               |       |
| Hypertension             | 144 (59.5%) | 141 (60.0%) | 0.912 |
| Dyslipidemia             | 66 (27.3%)  | 70 (29.8%)  | 0.543 |
| DM                       | 50 (20.7%)  | 37 (15.7%)  | 0.164 |
| AF                       | 121 (50.0%) | 119 (50.6%) | 0.889 |
| NIHSS score, median (IQR) | 18 (11–23) | 19 (14–24) | 0.026 |
| Diagnostic modality for occluded vessels | | | |
| MRA                      | 175 (72.3%) | 167 (71.1%) | 0.006 |
| CTA                      | 41 (16.9%)  | 58 (24.7%)  |       |
| DSA                      | 26 (10.7%)  | 10 (4.3%)   |       |
| Occlusion site            |               |               |       |
| ICA                      | 79 (32.6%)  | 79 (33.6%)  | 0.822 |
| MCA-M1                   | 101 (41.7%) | 97 (41.3%)  | 0.919 |
| MCA-M2–M3                | 46 (19.0%)  | 33 (14.0%)  | 0.145 |
| VA-BA                    | 24 (9.9%)   | 27 (11.5%)  | 0.579 |
| ACA                      | 2 (0.8%)    | 2 (0.9%)    | 0.976 |
| PCA                      | 1 (0.4%)    | 3 (1.3%)    | 0.301 |
| Etiology                 |               |               |       |
| CE                       | 163 (67.4%) | 158 (67.2%) | 0.021 |
| LAA                      | 49 (20.2%)  | 30 (12.8%)  |       |
| Dissection               | 7 (2.9%)    | 4 (1.7%)    |       |
| Other                    | 9 (3.7%)    | 19 (8.1%)   |       |
| Etiology unknown         | 14 (5.8%)   | 20 (10.2%)  |       |
| iv-rtPA                  |               |               |       |
| Administered             | 108 (44.6%) | 89 (37.9%)  | 0.206 |
| Not administered         | 134 (55.4%) | 108 (61.7%) |       |
| Unknown                  | 0           | 1 (0.4%)    |       |
| Anesthesia               |               |               |       |
| Local anesthesia         | 138 (57.0%) | 134 (57.0%) | 0.218 |
| Conscious sedatives      | 92 (38.0%)  | 79 (33.6%)  |       |
| General anesthesia       | 11 (4.5%)   | 18 (7.7%)   |       |
| Unknown                  | 1 (0.4%)    | 4 (1.7%)    |       |

ACA: anterior cerebral artery; AF: atrial fibrillation; BA: basilar artery; CE: cardioembolism; CTA: computed tomography angiography; DM: diabetes mellitus; DSA: digital subtraction angiography; ICA: internal carotid artery; iv-rtPA: intravenous recombinant tissue plasminogen activator; LAA: large artery atherosclerosis; MCA: middle cerebral artery; MRA: magnetic resonance angiography; mRS: modified Rankin Scale; PCA: posterior cerebral artery; VA: vertebral artery.
lower NIHSS score were predictors of delays in O2D time. In the present study, although NIHSS scores tended to be higher in 2020 than in 2019, O2D time was significantly longer in 2020, suggesting an association between COVID-19 outbreaks and delays in O2D time, especially in the first half of the year. The present study

Table 2. Outcomes.

|                  | 2019 (n = 242) | 2020 (n = 235) | p    |
|------------------|----------------|----------------|------|
| **Primary outcome** |                |                |      |
| O2D median (IQR), min | 105.0 (51.7–235.2) | 146.0 (51.0–360.0) | 0.034 |
| D2P median (IQR), min | 67.0 (47.0–97.2) | 75.0 (53.0–95.0) | 0.229 |
| mRS 0–2 at 90 days | 109 (45.0%) | 87 (37.0%) | 0.075 |
| **Secondary outcome** |                |                |      |
| D2N median (IQR), min | 62.5 (47.2–87.0) (n = 100) | 67.0 (53.0–82.0) (n = 82) | 0.410 |
| P2R median (IQR), min | 46.0 (31.0–73.5) (n = 190) | 47.5 (28.0–72.2) (n = 190) | 0.468 |
| O2R median (IQR), min | 246.0 (183.0–381.5) (n = 190) | 262.0 (195.0–480.0) (n = 190) | 0.033 |

| Number of passes | Unknown | 1 | 2 | 3 | >4 |        |
|------------------|---------|---|---|---|----|--------|
| 2019 (n = 242) | 4 (1.7%) | 121 (50.0%) | 48 (19.8%) | 45 (18.6%) | 24 (9.9%) | 5 (2.1%) |
| 2020 (n = 235) | 104 (44.3%) | 62 (26.4%) | 47 (20.0%) | 17 (7.2%) | 4 (1.7%) | 5 (2.1%) |

| mTICI grade | 2b–3 | 0–2a | Unknown |        |
|-------------|------|------|---------|--------|
| 2019 (n = 242) | 197 (81.4%) | 44 (18.2%) | 1 (0.4%) | 177 (72.9%) |
| 2020 (n = 235) | 188 (80.0%) | 43 (18.3%) | 4 (1.7%) | 173 (73.4%) |

| mRS score 0–2 at discharge |        |
|-----------------------------|--------|
| 2019 (n = 242) | 83 (34.3%) | 62 (26.4%) |
| 2020 (n = 235) | 80 (34.3%) | 59 (25.2%) |

| Death at 90 days |        |
|------------------|--------|
| 2019 (n = 212) | 24 (9.9%) | 35 (14.9%) |
| 2020 (n = 210) | 27 (12.9%) | 35 (16.7%) |

| Any ICH | ICH (+) | ICH (−) | Unknown |        |
|---------|---------|---------|---------|--------|
| 2019 (n = 212) | 72 (29.8%) | 161 (66.5%) | 9 (3.7%) | 193 (87.4%) |
| 2020 (n = 210) | 89 (37.9%) | 135 (57.4%) | 11 (4.2%) | 205 (92.9%) |

| sICH | sICH (+) | sICH (−) | Unknown |        |
|------|---------|---------|---------|--------|
| 2019 (n = 212) | 7 (2.9%) | 226 (93.4%) | 9 (3.7%) | 243 (105.0%) |
| 2020 (n = 210) | 12 (5.1%) | 212 (90.2%) | 11 (4.7%) | 245 (106.3%) |

Table 3. Pre-hospital time courses and time courses of transferred cases (2019 vs. 2020)

| Total case                  | 2019 (n = 242) | 2020 (n = 235) | p    |
|-----------------------------|----------------|----------------|------|
| **Pre-hospital time course** |                |                |      |
| Onset/LKW to EMS call, median (IQR), min | 36.5 (10.0–167.2) (n = 194) | 64.0 (8.5–289.5) (n = 185) | 0.209 |
| EMS call to arrival at the site, median (IQR), min | 8.0 (6.0–10.0) (n = 192) | 9.0 (7.0–12.0) (n = 183) | 0.005 |
| Arrival at the site to departure, median (IQR), min | 16.0 (13.0–19.7) (n = 192) | 16.5 (13.0–20.0) (n = 180) | 0.246 |
| Departure to door, median (IQR), min | 12.0 (8.0–15.2) (n = 194) | 12.0 (9.0–16.0) (n = 178) | 0.834 |
| **Cases transferred from another hospital** |                |                |      |
| Door-to-picture in H1, median (IQR), min | 26.0 (19.5–52.5) (n = 25) | 36.0 (21.2–54.2) (n = 36) | 0.352 |
| Door (H1) to departure (H1), median (IQR), min | 95.0 (61.0–117.0) (n = 25) | 113.5 (94.2–153.7) (n = 36) | 0.008 |
| Departure (H1) to door (H2), median (IQR), min | 17.0 (14.0–22.2) (n = 34) | 20.0 (13.0–30.0) (n = 47) | 0.576 |
| Door (H1) to door (H2), median (IQR), min | 112.0 (79.5–135.0) (n = 28) | 133.0 (106.0–171.0) (n = 37) | 0.008 |

| EMS: emergency medical service, H1: hospital transferred at first, H2: hospital secondary transferred for thrombectomy, LKW: last known well, NA: not available. |        |

 EMS: emergency medical service, H1: hospital transferred at first, H2: hospital secondary transferred for thrombectomy, LKW: last known well, NA: not available.
also revealed that (1) EMS call to arrival at the site door (H1) to departure (H1) and door (H1) to door (H2) times were significantly longer in 2020, that (2) O2D time or LKW time to EMS call was longer in 2020, although this difference was not significantly different, and that (3) there was no difference in EMS arrival at the site to departure. These findings suggest that the delays in O2D time in 2020 might have been caused by patients’ refraining from going to hospital as opposed to the difficulty of searching for a hospital with open beds. From April 7 to May 31, 2020, the Japanese government declared a state of emergency and asked people to self-quarantine, which might have delayed the decisions of patients to make emergency calls or go to the hospital. At the beginning of the pandemic, less information was available about COVID-19 and guidelines for emergency medicine during the pandemic, which might have caused confusion in medical settings or EMS. In addition, medical staff

suddenly had to wear unfamiliar personal protective equipment, which could help explain the delay in door (H1) to door (H2) time.

The difference in D2P time in the subgroup analysis from October to December 2020, during the peak of the third wave, cannot fully be explained by other predictors (e.g., transfer, iv-rtPA, diagnostic modality for occluded vessels, anesthesia) since these factors did not indicate any imbalances; and although CTA may require less time than MRA, the diagnostic modality for occluded vessels (MRA or CTA) was not found to be a predictor of D2P

| Table 4. Outcomes of the subgroup analysis |
|-------------------------------------------|
| January to March                          |
| number                                    | 66 | 74 | -              |
| O2D, median (IQR), min                    | 84.5 (51.0–160.7) | 140.0 (47.7–408.5) | 0.025 |
| D2P, median (IQR), min                    | 66.5 (47.7–93.5) | 69.0 (51.0–94.5) | 0.832 |
| mRS 0–2 at 90 days                        | 35 (53.0%) | 29 (39.2%) | 0.101 |
| April to June                             |
| number                                    | 60 | 61 |               |
| O2D, median (IQR), min                    | 105.5 (51.5–224.0) | 155.0 (52.5–485.0) | 0.025 |
| D2P, median (IQR), min                    | 66.5 (47.2–96.5) | 67.0 (52.0–90.5) | 0.832 |
| mRS 0–2 at 90 days                        | 26 (43.3%) | 23 (37.7%) | 0.528 |
| July to September                         |
| number                                    | 56 | 51 |               |
| O2D, median (IQR), min                    | 105.5 (50.2–224.0) | 154.0 (52.0–258.0) | 0.521 |
| D2P, median (IQR), min                    | 71.0 (49.5–103.0) | 68.0 (53.0–91.0) | 0.609 |
| mRS 0–2 at 90 days                        | 24 (42.9%) | 16 (31.4%) | 0.220 |
| October to December                       |
| number                                    | 60 | 49 |               |
| O2D, median (IQR), min                    | 143.5 (53.0–301.2) | 111.0 (48.5–316.5) | 0.918 |
| D2P, median (IQR), min                    | 62.5 (42.0–100.2) | 82.0 (63.0–109.0) | 0.022 |
| mRS 0–2 at 90 days                        | 24 (40.0%) | 19 (38.8%) | 0.896 |

D2P: door-to-puncture time; min: minutes, mRS: modified Rankin Scale; O2D: onset-to-door time.

| Table 5. Results of multivariable logistic regression analysis for longer onset-to-door (O2D) time |
|-----------------------------------------------|
| OR 95% CI p |
| LKW               | 17.8 10.4–30.3 < 0.001 |
| Transferred from another hospital             | 21.2 9.98–45.1 < 0.001 |
| Male                                         | 1.17 0.70–1.93 0.537 |
| Pre-mRS 1                                     | 0.39 0.18–0.83 0.015 |
| Pre-mRS 2                                     | 1.51 0.66–3.46 0.328 |
| Lower NIHSS                                   | 0.95 0.92–0.97 0.001 |
| 2020                                          | 1.72 1.06–2.82 0.028 |
| CI: confidence interval; LKW: last-known-well; mRS: modified Rankin Scale; NIHSS: National Institute of Health Stroke Scale; OR: odds ratio. |

| Table 6. Results of multivariable logistic regression analysis for mRS score 0–2 at 90 days |
|-----------------------------------------------|
| OR 95% CI p |
| Older age                                      | 0.95 0.93–0.97 < 0.001 |
| Pre-mRS 1                                      | 0.48 0.23–1.00 0.053 |
| Pre-mRS 2                                      | 0.31 0.12–0.78 0.013 |
| Higher NIHSS                                   | 0.90 0.87–0.93 < 0.001 |
| DM                                            | 0.39 0.20–0.77 0.007 |
| ICA occlusion                                  | 0.71 0.41–1.22 0.218 |
| iv-rtPA                                       | 1.51 0.87–2.61 0.135 |
| O2D                                           | 0.99 0.99–1.00 0.045 |
| D2P                                           | 1.00 0.99–1.00 0.939 |
| P2R                                           | 0.98 0.97–0.99 < 0.001 |
| mTICI ≥ 2b                                     | 9.62 0.92–100.2 0.058 |
| Any ICH                                       | 0.29 0.17–0.80 < 0.024 |
| Year (2020)                                    | 0.86 0.52–1.42 0.558 |
| CI: confidence interval; DM: diabetes mellitus; D2P: door to puncture time; ICA: internal carotid artery; ICH: intracranial hemorrhage; iv-rtPA: intravenous recombinant tissue plasminogen activator; mRS: modified Rankin Scale; mTICI: modified TICI grade; NIHSS: National Institute of Health Stroke Scale; O2D: onset-to-door time; OR: odds ratio; P2R: puncture-to-recanalization time. |
time in a previous study; thus, it could be explained by the different protocols and systems in each hospital, information on which was not collected in the present study. However, D2P time was not significantly different for the entire study period, so we may conclude that the COVID-19 pandemic did not affect the initial management in each hospital.

The impact of COVID-19 on functional outcomes after MT remains unclear. Despite higher NIHSS scores in 2020, mRS score 0–2 at 90 days did not differ between 2019 and 2020. Patients with a severe case of COVID-19 sometimes present with large-vessel stroke, and a previous report suggested that such patients may be at increased risk of AIS and in-hospital mortality. In Tokyo, although we did not have complete data throughout 2020, COVID-19-related stroke was found in only 0.03% of the patients enrolled in TREAT from February to July 2020. Fewer patients have been diagnosed with COVID-19 Japan than in the United States and other European countries (Fig. 1), and this could be related to the smaller number of patients with severe COVID-19-related stroke, which would have less impact on functional outcomes. Although the present study could not enroll all stroke patients in all hospitals in Tokyo, it seems reasonable to conclude that MT could still be performed safely and effectively in Tokyo, despite the pandemic.

Our study has several limitations. First, we did not include patients treated by best medical treatment, which could have led to a selection bias. In addition, we could not estimate the O2D time of these patients, which would cause a difference from the real-world O2D time for patients with AIS in Tokyo. Second, we excluded about 30% of the eligible patients based on the exclusion criteria, and thus, our study sample could differ from real-world data. Third, we did not collect the AIS protocol in each hospital, which relates to D2P time, or the presence of COVID-19, which relates to functional outcomes. Finally, this was a multicenter study conducted in the Tokyo Metropolitan Area, which could limit the generalizability of the results to other populations.

Conclusions

The results of this study indicated that O2D time was significantly longer in 2020 than in 2019 and may have been affected by the COVID-19 pandemic. However, D2P time and mRS score 0–2 at 90 days were not significantly different between 2019 and 2020. Although we could not enroll all stroke patients in Tokyo in the present study, we can reasonably conclude that despite the COVID-19 pandemic, the initial management of patients with AIS was effective and MT was well performed.

Funding

This registry was partially supported by Taiju Life Social Welfare Foundation.

Declaration of Competing Interest

Yoshiaki Shiokawa has received research grants from AbbVie GK and ONO Pharmaceutical CO., LTD. Teruyuki Hirano has received honoraria from Bayer, Boehinger-Ingelheim, Bristol-Myers Squibb, Daiichi-Sankyo, Otsuka Pharma, Pfizer, and Sanofi. All the other authors have nothing to disclose.

Acknowledgment: We are grateful to Dr Sei Harada, Department of Preventive Medicine and Public Health, Keio University School of Medicine, Tokyo, Japan, for discussion and instruction of statistical method; measurement of ICC and fixed effect method.

References

1. Teo KC, Leung WCY, Wong YK, et al. Delays in stroke onset to hospital arrival time during COVID-19. Stroke 2020;51:2228-2231.
2. Tejada Meza H, Lambea Gil A, Sancho Saldana A, et al. Ischemic stroke in the time of coronavirus disease 2019. Eur J Neurol 2020;27:1788-1792.
3. Yang B, Wang T, Chen J, et al. Impact of the COVID-19 pandemic on the process and outcome of thrombectomy for acute ischemic stroke. J Neurointerv Surg 2020;12:664-668.
4. Schirmer CM, Ringer AJ, Arthur AS, et al. Delayed presentation of acute ischemic strokes during the COVID-19 crisis. J Neurointerv Surg 2020;12:639-642.
5. Nogueira RG, Abdalkader M, Qureshi MM, et al. Global impact of COVID-19 on stroke care. Int J Stroke 2021;16:573-584.
6. Ota T, Shigeta K, Amano T, et al. Regionwide retrospective survey of acute mechanical thrombectomy in Tama, Suburban Tokyo: a preliminary report. J Stroke Cerebrovasc Dis 2018;27:3350-3355.
7. Zaidat OO, Yoo AJ, Khatri P, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. Stroke 2013;44:2650-2663.
8. Ishihara H, Oka F, Oku T, et al. Safety and time course of drip-and-ship in treatment of acute ischemic stroke. J Stroke Cerebrovasc Dis 2017;26:2477-2481.
9. Lee EJ, Kim SJ, Bae J, et al. Impact of onset-to-door time on outcomes and factors associated with late hospital arrival in patients with acute ischemic stroke. PLoS One 2021;16:e0247829.
10. Deb-Chatterji M, Pinischmidt H, Flottmann F, et al. Stroke patients treated by thrombectomy in real life differ from cohorts of the clinical trials: a prospective observational study. BMC Neurol 2020;20:81.
11. Lu GD, Ren ZQ, Zhang JX, et al. Effects of diabetes mellitus and admission glucose in patients receiving mechanical thrombectomy: a systematic review and meta-analysis. Neurocrit Care 2018;29:426-434.
12. Mohammaden MH, Stapleton CJ, Brunozzi D, et al. Predictors of poor outcome despite successful mechanical thrombectomy of anterior circulation large vessel occlusions within 6 h of symptom onset. Front Neurol 2020;11:907.
14. Maingard J, Shvarts Y, Motyer R, et al. Outcomes of endovascular thrombectomy with and without bridging thrombolysis for acute large vessel occlusion ischaemic stroke. Intern Med J 2019;49:345-351.
15. Matsuo R, Yamaguchi Y, Matsushita T, et al. Association between onset-to-door time and clinical outcomes after ischemic stroke. Stroke 2017;48:3049-3056.
16. Atchaneeyasakul K, Liebeskind DS, Jahan R, et al. Efficient multimodal MRI evaluation for endovascular thrombectomy of anterior circulation large vessel occlusion. J Stroke Cerebrovasc Dis 2020;29:105271.
17. Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med 2020;382:e60.
18. Escalard S, Chalumeau V, Escalard C, et al. Early brain imaging shows increased severity of acute ischemic strokes with large vessel occlusion in COVID-19 patients. Stroke 2020;51:3366-3370.