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Evaluation of Workflow Delays in Stroke Reperfusion Therapy: A Comparison between the Year-Long Pre-COVID-19 Period and the with-COVID-19 Period

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Aim: We evaluated the delay in stroke reperfusion therapy between the pre-coronavirus disease 2019 (COVID-19) period and the with-COVID-19 period, and compared this delay between each phase of the with-COVID-19 period.

Methods: Patients with acute ischemic stroke (AIS) undergoing intravenous thrombolysis and/or mechanical thrombectomy were selected from our single-center prospective registry. The time to perform reperfusion therapy were compared between patients admitted from March 2019 to February 2020 (pre-COVID-19 group) and those from March 2020 to February 2021 (with-COVID-19 group). Patients in the with-COVID-19 group were further divided into three 4-month-long subgroups (first-phase: March to June 2020; second-phase: July to October 2020; third-phase: November 2020 to February 2021), and the time delay of reperfusion therapy were compared between these subgroups.

Results: Of 1,260 patients with AIS hospitalized in the study period, 265 patients were examined. Compared with the pre-COVID-19 group (133 patients; median age, 79 years), the with-COVID-19 group (132 patients; median age, 79 years) had a longer median door-to-imaging time (25 min vs. 27 min, $P=0.04$), and a longer door-to-groin puncture time (65 min vs. 72 min, $P=0.02$). In the three 4-month-long subgroups, the median door-to-needle time (49 min, 43 min, and 38 min, respectively; $P=0.04$) and door-to-groin puncture time (83 min, 70 min, and 61 min, $P<0.01$, respectively) decreased significantly during the with-COVID-19 period.

Conclusions: The delay in reperfusion therapy increased during the with-COVID-19 period compared with the pre-COVID-19 period. However, the door-to-needle time and door-to-groin puncture time decreased as time elapsed during the with-COVID-19 period.

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Key words: Coronavirus disease 2019, Ischemic stroke, Reperfusion therapy, Workflow

Introduction

In December 2019, emergence of the coronavirus disease 2019 (COVID-19) had devastating consequences worldwide[1-2]. Since then, the COVID-19 pandemic has led to an unprecedented paradigm shift in medical care. Healthcare providers have faced a frontline battle with the COVID-19 pandemic for over a year, and medical staff engaged in stroke unit care and reperfusion therapy workflows are no exception. Healthcare providers continue to be exposed to the terrifying threat of COVID-19. Stroke

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care staff are faced with the critical challenge of providing high-quality emergency reperfusion therapy, including intravenous thrombolysis (IVT) and/or mechanical thrombectomy (MT), while maximizing their efforts to minimize infectious exposure. To prevent the threat of exposure, the reperfusion therapy workflow was revised. Several reports of modified reperfusion therapy workflows, including protocols designed to protect against COVID-19 transmission (Protected Code Stroke [PCS])[3] and the Guidance Statement for large vessel occlusion stroke in the era of COVID-19 [4-7], have been reported. A change in the time to reperfusion therapy after the COVID-19 pandemic was determined in recent reports[8-21], but the findings were heterogeneous. Furthermore, few studies have investigated the delay in reperfusion therapy during the COVID-19 pandemic.

The number of patients affected by COVID-19 in Japan is shown in **Supplemental Fig. 1**. In April 2020, a state of emergency was declared for the first wave of COVID-19 infection (the first-phase). A domestic PCS was published by the Japan Stroke Society[22], and a novel institutional stroke protocol for the COVID-19 pandemic was implemented at our institution[20]. The number of COVID-19-positive cases increased again after the state of emergency was lifted at the end of May 2020 (the second-phase). The third wave began in November 2020, and a state of emergency was re-declared in January 2021 (the third-phase).

Aims

We compared the delay in stroke reperfusion therapy between the year-long pre-COVID-19 and with-COVID-19 periods. We also compared the delay in reperfusion therapy between each phase of the with-COVID-19 period. Differences in the first-used imaging modality and the delay in reperfusion therapy off-hours were also compared between the pre-COVID-19 and with-COVID-19 periods.

Methods

Study Population

This was a single-center, observational, cohort study performed at a comprehensive stroke center in Suita City in Japan (north sub-urban city of metropolitan Osaka), which has a total population of 375,000. All patients with acute ischemic stroke (AIS) admitted to our institution within 7 days from symptom onset or "last known well" were prospectively registered in the National Cerebral and Cardiovascular Center (NCVC) Stroke Registry. Data from March 2019 to February 2021 were retrospectively reviewed, and patients admitted within 24 hours of symptom onset and who were treated with reperfusion therapy, including IVT and/or MT, were included. The polymerase chain reaction test was used to determine severe acute respiratory syndrome coronavirus 2 positivity.

Treatments

Patients were treated with IVT using alteplase at 0.6 mg/kg according to the standard of care protocol in Japan[23]. All endovascular procedures were performed by neurointerventionalists certified by the Japanese Society for Neuroendovascular Therapy according to American Heart Association/American Stroke Association guidelines[24] and Guidelines for Mechanical Thrombectomy in Japan[25].

Clinical Data Collection

Baseline clinical characteristics for the following variables were collected from the NCVC Stroke Registry: sex; age; pre-stroke modified Rankin Scale (mRS) score; medical history, including hypertension, dyslipidemia, diabetes mellitus, current smoking, ischemic stroke, and atrial fibrillation; systolic blood pressure on admission; baseline National Institutes of Health Stroke Scale (NIHSS) score; Alberta Stroke Program Early Computed Tomography Score (ASPECTS) on computed tomography (CT) or diffusion-weighted imaging (DWI) at admission; internal carotid artery, middle cerebral artery M1 segment, or basilar artery occlusion; time intervals (onset-to-door [OTD] time, door-to-imaging [DTI] time, door-to-needle [DTN] time, door-to-groin puncture [DTP] time, imaging-to-groin puncture time, groin puncture-to-recanalization time); treatment profile (IVT, MT, or bridging therapy [IVT plus MT]); causative mechanism of stroke; and functional outcomes assessed by the mRS at 3 months. ASPECTS measurement by DWI was preferentially adopted over measurement by CT. Occlusion sites were determined using CT angiography, magnetic resonance angiography, or digital subtraction angiography at admission. The time of onset was defined as either the time when symptoms appeared or when the patient was last known well if the time of symptom onset was unknown. The causative mechanism of stroke was determined according to the Trial of ORG 10172 in Acute Stroke Treatment criteria by board-certified stroke neurologists.

Statistical Analyses

Data are summarized as median (interquartile range [IQR]) for continuous variables and frequencies

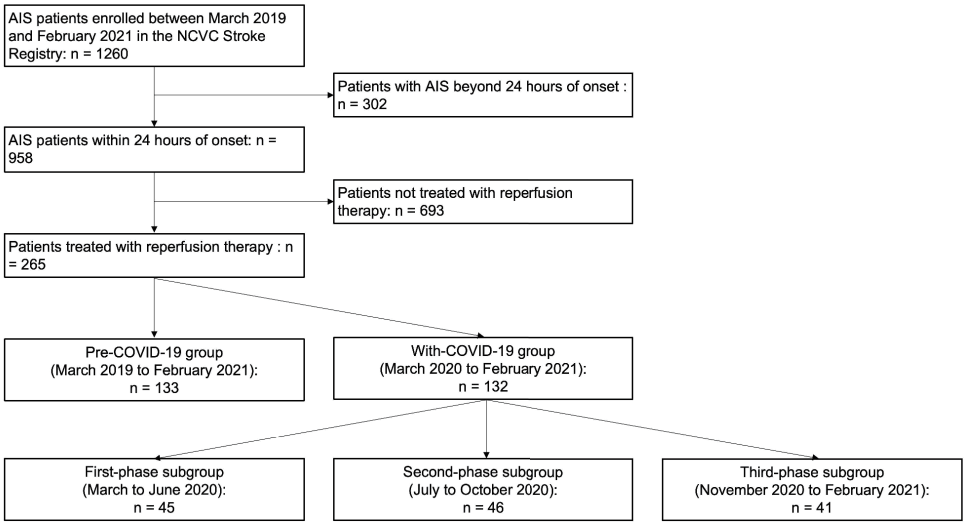

Fig. 1. Study flowchart

Abbreviations: AIS, acute ischemic stroke; COVID-19, coronavirus disease 2019; NCVC, National Cerebral and Cardiovascular Center

and percentages for categorical variables. Patients were divided into two year-long groups: the pre-COVID-19 group (March 2019 to February 2020) and the with-COVID-19 group (March 2020 to February 2021). The clinical characteristics, outcomes, and delays in reperfusion therapy were compared between groups using the Mann–Whitney *U* test or Fisher's exact test, as appropriate. Patients in the with-COVID-19 group were further divided into three 4-month-long subgroups according to the three COVID-19 waves in Japan (first-phase subgroup: March to June 2020; second-phase subgroup: July to October 2020; third-phase subgroup: November 2020 to February 2021), and delays in reperfusion therapy in the three subgroups were compared using the Kruskal–Wallis test. Delays in reperfusion therapy off-hours and on-hours were also compared between the pre-COVID-19 period and the with-COVID-19 period. On-hours was defined when patients arrived at hospital between 9 am and 5 pm Monday to Friday, while off-hours was defined when patients arrived outside of the above timeframes. A Cochran–Armitage test was performed to evaluate the statistical significance of the trend in first-used imaging modality (magnetic resonance imaging [MRI] or CT). Moreover, delays in reperfusion therapy were analyzed between the three subgroups in the with-COVID-19 period using the Kruskal–Wallis test for each first-used imaging modality. All reported *P* values were two-tailed, and a *P* value of <0.05 was considered statistically significant. All analyses were performed using Stata/IC software, version 16.1 (Stata Corp. LP., College Station, TX).

Results

Of 1,260 patients enrolled into the NCVC Stroke Registry during the study period, 265 patients (93 females, 172 males) (median age, 79 years; median NIHSS score, 12) who underwent reperfusion therapy were included. Of these, 133 were allocated to the pre-COVID-19 group, while 132 were allocated to the with-COVID-19 group (**Fig. 1**). All patients were COVID-19-negative, with the exception of one patient in the with-COVID-19 group who was COVID-19-positive. The number of overall AIS admissions and patients with AIS undergoing IVT or MT at the NCVC, as well as the number of new patients with COVID-19 in Suita City between March 2020 and February 2021, are shown in **Fig. 2**.

The baseline characteristics and clinical outcomes of patients are shown in **Table 1**. The with-COVID-19 group less frequently underwent MRI as the first-used imaging tool compared with the pre-COVID-19 group (49% vs. 83%, respectively; $P<0.01$). The time delay in reperfusion therapy was shown in **Table 2 and Fig. 3**. The with-COVID-19 group had a longer median DTI time (25 min vs. 27 min, respectively; $P<0.01$), a longer median DTP time (65 min vs. 72 min, respectively; $P=0.02$), and a lower rate of reaching a target DTP time of ≤ 75 min (48% vs. 27%, respectively; $P<0.01$). The DTN time and DTP time decreased as time elapsed during the with-COVID-19 period among the three 4-month-long subgroups (DTN time: 46 min, 43 min, and 38 min, respectively; $P=0.04$; DTP time: 83 min, 70 min, and 61 min, respectively; $P<0.01$). The time delays for

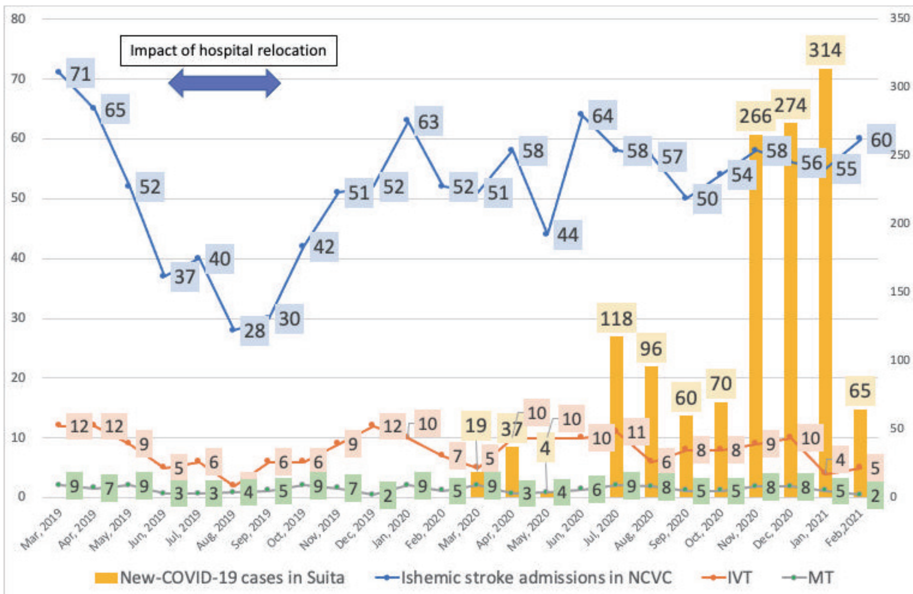

Fig. 2. Monthly volume of new COVID-19 cases in Suita City and the number of emergency medical service transfers, stroke admissions, and reperfusion therapy cases at the NCVC

Abbreviations: COVID-19, coronavirus disease 2019; IVT, intravenous thrombolysis; MT, mechanical thrombectomy; NCVC, National Cerebral and Cardiovascular Center.
New-COVID-19 cases in Suita City edited based on openly available data from Suita City, Osaka Prefecture < https://www.city.suita.osaka.jp/coronavirus/_102520.html >.

each type of reperfusion therapy (IVT only, MT only, and bridging therapy) are shown in **Fig. 4**. A similar reduction in time delay was observed in patients undergoing IVT only (median DTI time: 30 min, 26 min, and 26 min, respectively, $P=0.05$; DTN time: 54 min, 45 min, and 38 min, respectively, $P=0.02$) compared with those undergoing bridging therapy (median DTP time: 87 min, 70 min, and 59 min, respectively; $P<0.01$). For on-hours admissions, DTI time and DTP time in the with-COVID-19 period were longer compared with the respective values in the pre-COVID-19 period (median DTI time: 29 min vs. 25 min, respectively, $P<0.01$; DTP time: 72 min vs. 62 min, respectively, $P=0.01$) **(Fig. 5)**. In the with-COVID-19 period, the proportion of patients who underwent CT as the first-used imaging modality gradually increased (Cochran–Armitage test: $P<0.01$) **(Fig. 6)**. The DTN and DTP times decreased as time elapsed during the with-COVID-19 period, regardless of the choice of first-used imaging modality. There was no difference in time delay between patients undergoing CT and those undergoing MRI **(Fig. 7)**.

Discussion

Our results show that the time delay in stroke reperfusion therapy in the year-long with-COVID-19 period were generally longer compared with the preceding year-long pre-COVID-19 period, especially DTI time, DTN time, and DTP time. However, DTN time and DTP time decreased as time elapsed during the with-COVID-19 period.

Both pre-hospital and in-hospital delays impede prompt hyperacute stroke care. In the present study, OTD time was a median of 29 minutes longer in the with-COVID-19 period compared with the pre-COVID-19 period, although this difference was not statistically significant. Other studies reported an increase in OTD time after the COVID-19 pandemic[13, 26, 27]. The causes of a delay in in-hospital care in the with-COVID-19 period include 1) the time required for the standard personal protective equipment, 2) the time taken to perform a COVID-19 antigen test if needed, 3) the time taken to secure the delivery flow-line from the emergency room to the imaging room/angiography suite and to prepare the angiography suite to avoid contact between patients with suspected COVID-19 and other patients or medical staff, and 4) potential fear of medical staff of contracting COVID-19. The present study indicates that these factors increased the time delay early after the beginning of the pandemic. The present study also suggests that adaptation of medical staff to stroke treatment during the COVID-19 pandemic through

Table 1. Comparison of baseline characteristics and clinical outcomes of patients between the year-long pre-COVID-19 and with-COVID-19 periods

Baseline characteristics	All ($n=265$)	Pre-COVID-19 period ($n=133$)	With-COVID-19 period ($n=132$)	*P*-value
	Mar 2019 to Feb 2021	Mar 2019 to Feb 2020	Mar 2020 to Feb 2021	
Women, *n* (%)	93 (35)	53 (40)	40 (31)	0.16
Age, median (IQR), years	79 [69–85]	79 [71–84]	79 [67–86]	0.95
Prestroke mRS score, median (IQR)	0 [0–2]	0 [0–2]	0 [0–2]	0.86
Baseline NIHSS score, median (IQR)	12 [6–22]	11 [5–21]	15 [6–22]	0.20
SBP on admission, median (IQR), mmHg	154 [140–178]	154 [140–178]	155 [139–178]	0.98
Medical history				
Hypertension, *n* (%)	183 (70)	98 (73)	85 (66)	0.23
Dyslipidemia, *n* (%)	126 (48)	74 (55)	52 (40)	0.02
Diabetes mellitus, *n* (%)	55 (21)	29 (22)	26 (20)	0.80
Congestive heart failure, *n* (%)	51 (20)	24 (18)	27 (21)	0.53
Ischemic stroke, *n* (%)	52 (20)	28 (21)	24 (19)	0.65
Current smoking, *n* (%)	49 (19)	28 (21)	21 (16)	0.30
Atrial fibrillation, *n* (%)	122 (46)	56 (42)	66 (51)	0.15
Ischemic heart disease, *n* (%)	33 (13)	16 (12)	17 (13)	0.85
Imaging				
MRI, *n* (%)	174 (66)	111 (83)	63 (49)	<0.01
CT, *n* (%)	90 (34)	23 (17)	67 (52)	<0.01
ASPECTS, median (IQR)*	9 [7–10]	9 [7–10]	10 [7–10]	0.40
ASPECTS on DWI, median (IQR)	9 [7–10] ($n=178$)	9 [7–10] ($n=111$)	9 [7–10] ($n=67$)	0.29
ASPECTS on CT, median (IQR)	10 [8–10] ($n=87$)	10 [10–10] ($n=22$)	10 [8–10] ($n=65$)	0.01
Occluded vessels				
Internal carotid artery, *n* (%)	39 (15)	21 (16)	18 (14)	0.73
M1 segment of middle cerebral artery, *n* (%)	66 (25)	26 (19)	40 (31)	0.05
Basilar artery, *n* (%)	10 (3.8)	7 (5.2)	3 (2.3)	0.34
Treatment profile				
Intravenous thrombolysis, *n* (%)	192 (72)	96 (71)	96 (73)	0.78
Mechanical thrombectomy, *n* (%)	145 (55)	71 (54)	73 (57)	0.62
Bridging therapy, *n* (%)	72 (27)	33 (25)	39 (30)	0.34
Stroke causative mechanism				0.75
Large-artery atherosclerosis, *n* (%)	34 (13)	18 (13)	16 (12)	
Cardioembolism, *n* (%)	133 (50)	65 (49)	68 (52)	
Small-vessel disease, *n* (%)	11 (4.2)	4 (3.0)	7 (5.4)	
Other, n (%)	39 (15)	20 (15)	19 (15)	
Undetermined, *n* (%)	47 (18)	27 (20)	20 (15)	
Clinical outcome				
mRS score 0–2 at 3 months, *n* (%)	113 (44)	65 (49)	48 (39)	0.13
Death within 3 months, *n* (%)	16 (6.2)	12 (9.0)	4 (3.2)	0.07

Numbers are presented as *n* (%) or median [IQR], as appropriate. Intergroup comparisons were made using the Wilcoxon rank-sum test or Fisher's exact test, as appropriate.

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; COVID-19, coronavirus disease 2019; CT, computed tomography; DWI, diffusion-weighted imaging; IQR, interquartile range; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

*ASPECTS was measured by magnetic resonance imaging DWI in principle, with CT as an option.

Table 2. Time delay of reperfusion therapy between the year-long pre-COVID-19 and the with-COVID-19 periods and between subgroups stratified by COVID-19 phase

	Pre-COVID-19 period ($n = 133$)	With-COVID-19 period ($n = 132$)	*P*-value	First-phase subgroup ($n = 45$)	Second-phase subgroup ($n = 46$)	Third-phase subgroup ($n = 41$)	*P*-value*
Period	Mar 2019 to Feb 2020	Mar 2020 to Feb 2021		Mar to Jun 2020	Jul to Oct 2020	Nov 2020 to Feb 2021	
Time intervals, median (IQR), min							
Onset-to-door time, median (IQR), min	86 [51–180]	113 [49–202]	0.32	87 [43–168]	109 [59–199]	122 [55–368]	0.25
Door-to-imaging time, median (IQR), min	25 [20–31] ($n = 129$)	27 [22–35] ($n = 128$)	<0.01	29 [25–41]	27 [22–33]	26 [21–37]	0.26
Door-to-needle time, median (IQR), min**	40 [33–52] ($n = 95$)	43 [37–58] ($n = 97$)	0.02	46 [37–66] ($n = 35$)	43 [38–57] ($n = 35$)	38 [35–43] ($n = 27$)	0.04
Door-to-needle time ≤ 60 minute, (%)**	82 (86) ($n = 95$)	77 (79) ($n = 97$)	0.61	25 (40) ($n = 35$)	27 (56) ($n = 35$)	24 (100) ($n = 24$)	0.88
Door-to-needle time ≤ 45 minute, (%)**	55 (58) ($n = 95$)	55 (57) ($n = 97$)	1.00	14 (40) ($n = 35$)	20 (59) ($n = 35$)	21 (88) ($n = 24$)	0.16
Door-to-groin puncture time, median (IQR), min§	65 [50–83] ($n = 71$)	72 [61–84] ($n = 74$)	0.02	83 [75–91] ($n = 22$)	70 [63–83] ($n = 28$)	61 [51–71] ($n = 24$)	0.005
Door-to-groin puncture time ≤ 60 min, (%)§	34 (48) ($n = 71$)	20 (27) ($n = 74$)	0.01	5 (23) ($n = 22$)	5 (18) ($n = 28$)	10 (42) ($n = 24$)	0.26
Door-to-groin puncture time ≤ 75 min, (%)§	50 (70) ($n = 71$)	39 (53) ($n = 74$)	0.04	10 (45) ($n = 22$)	16 (57) ($n = 28$)	14 (58) ($n = 24$)	0.35
Imaging-to-groin puncture time, median (IQR), min	36 [28–49] ($n = 71$)	46 [32–61] ($n = 74$)	0.03	53 [43–60] ($n = 22$)	45 [35–51] ($n = 28$)	30 [21–40] ($n = 24$)	0.005
Groin puncture-to-recanalization time, median (IQR), min	37 [27–70] ($n = 65$)	37 [22–70] ($n = 68$)	0.17	45 [27–73] ($n = 22$)	38 [21–115] ($n = 27$)	36 [22–62] ($n = 19$)	0.90

Numbers are presented as *n* (%) or median [IQR], as appropriate. Intergroup comparisons were performed using the Wilcoxon rank-sum test, Fisher's exact test, or the Kruskal–Wallis test, as appropriate. Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range.
*Kruskal–Wallis test
*Only patients who underwent intravenous thrombolysis were included. Drip cases were excluded.
§Only patients who underwent or attempted to undergo mechanical thrombectomy were included.

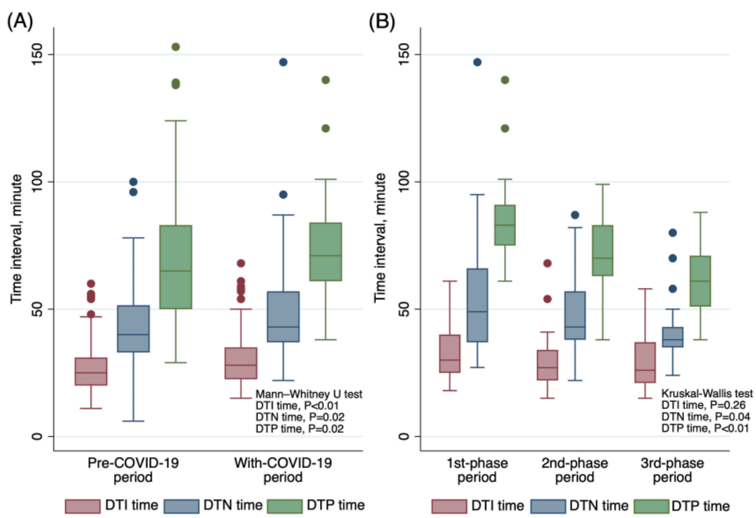

Fig. 3. Time delay in reperfusion therapy for patients with AIS

Time delay in reperfusion therapy for AIS between the pre-COVID-19 and the with-COVID-19 periods (A) and between each phase of the with-COVID-19 period (B).
Box-and-whisker plots of DTI time, DTN time, and DTP time. Boxes indicate interquartile range; whiskers indicate extreme values; horizontal lines in each box indicate median values; and horizontal lines indicate mean values.
Abbreviations: AIS, acute ischemic stroke; COVID-19, coronavirus disease 2019; DTI, door-to-imaging; DTN, door-to-needle; DTP, door-to-groin puncture

training and experience gradually shortened the delay. Some previous studies support the delay in reperfusion therapy during the first months of the COVID-19 pandemic[18-20, 26, 28], while others do not[8, 9, 14-19, 29]. Such divergence might be due to differences in the severity of infectious spread and PCS strategy.

A change in the number of patients with emergent stroke after the COVID-19 pandemic seemed to also influence the status of hyperacute stroke care. The number reportedly decreased by two-

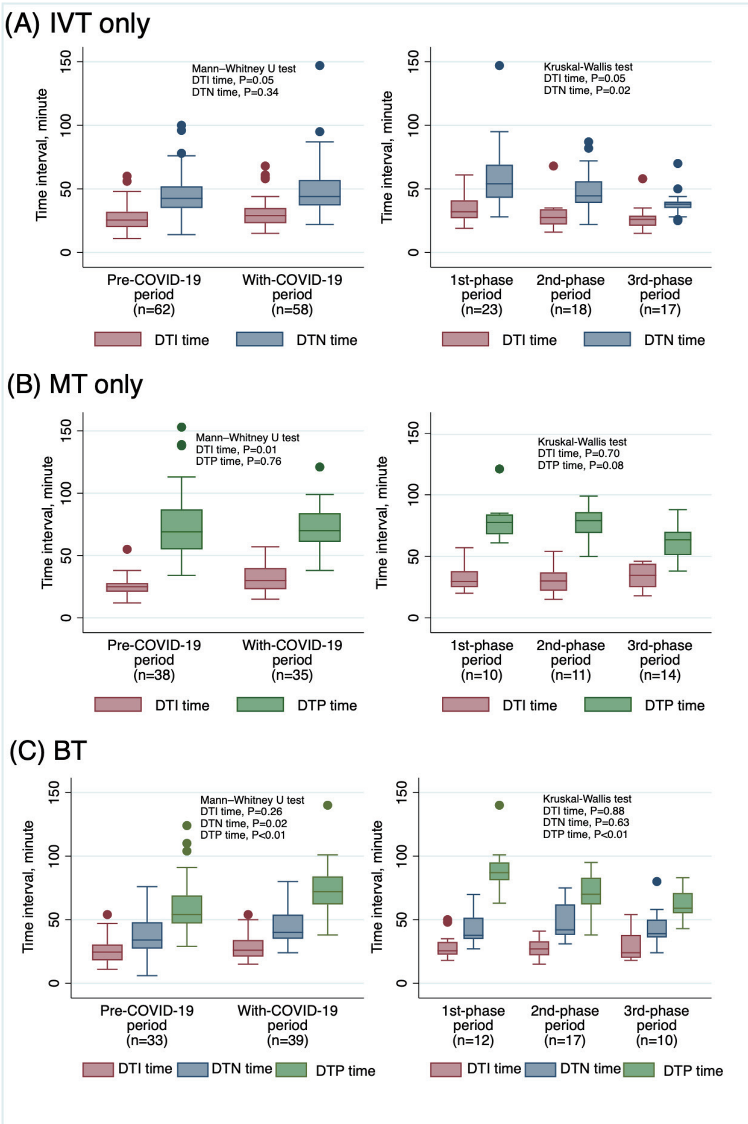

Fig. 4. Time delay of each type of reperfusion therapy

Time delay in IVT only (A), MT (B), and BT (C) for AIS between the pre-COVID-19 and the with-COVID-19 periods and between each phase of the with-COVID-19 period. Box-and-whisker plots of DTI time, DTN time, and DTP time. Boxes indicate interquartile range; whiskers indicate extreme values; horizontal lines in each box indicate median values; and horizontal lines indicate mean values. Bridging therapy consisted of IVT and MT.
Abbreviations: BT, bridging therapy; COVID-19, coronavirus disease 2019; DTI, door-to-imaging; DTN, door-to-needle; DTP, door-to-groin puncture; IVT, intravenous thrombolysis; MT, mechanical thrombectomy.

thirds in Western countries[8, 13, 27]. Although the number of overall patients with AIS decreased somewhat early on in the with-COVID-19 period, the total number of patients undergoing reperfusion therapy per year did not change between the pre-COVID-19 and with-COVID-19 periods. This might be partly because of a much smaller number of patients infected with COVID-19 in Japan compared with Western countries.

Interestingly, there were no increases in the time delay of reperfusion therapy after the COVID-19 pandemic in off-hours practice. This might be due to the lower risk of contact with other patients and medical staff while transporting patients to the angiography suite compared with on-hours practice. The change in the first-used imaging modality from MRI to CT at our institution was mainly due to the inconvenience of cleaning and ventilating MRI equipment for complete disinfection[20]. Ventilation of CT rooms is much easier. This change in the first-used

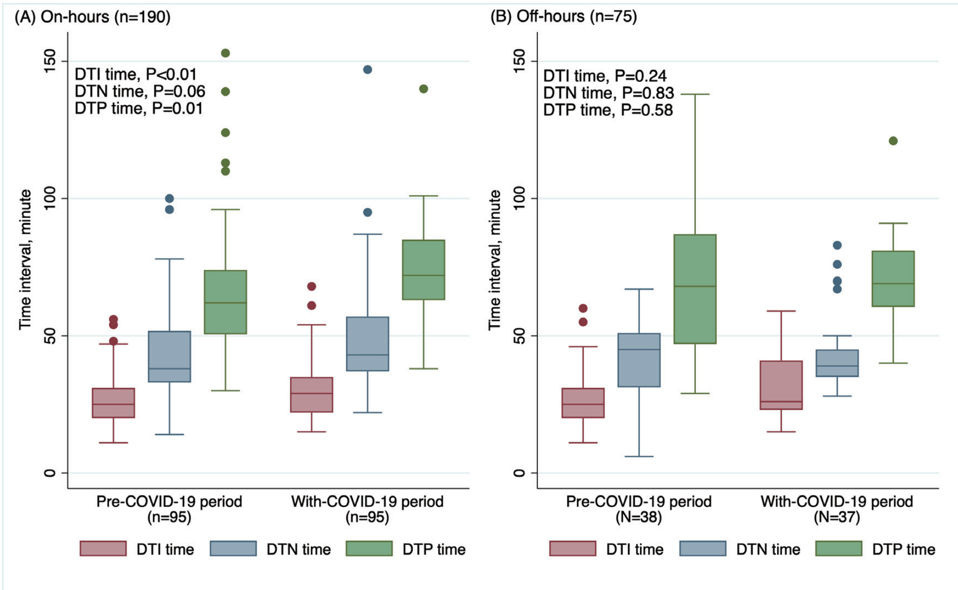

Fig. 5. Time delay of reperfusion therapy in on-hours and off-hours practice

Time delay of reperfusion therapy during on-hours (A) or off-hours (B) practice.
Abbreviations: COVID-19, coronavirus disease 2019; DTI, door-to-imaging; DTN, door-to-needle; DTP, door-to-groin puncture.

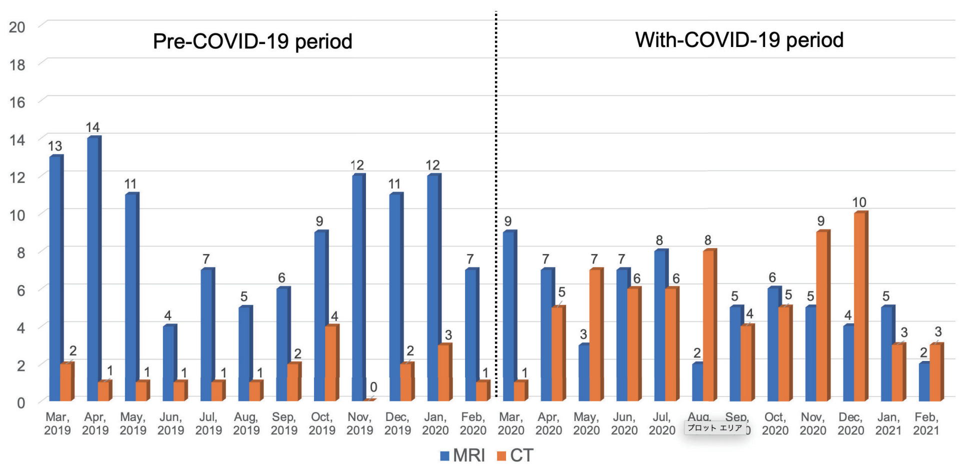

Fig. 6. Monthly transition in the first-used imaging modality between the pre-COVID-19 and with-COVID-19 periods

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; MRI, magnetic resonance imaging.

imaging modality did not affect time reduction.

One limitation of this study was that it adopted a single-center study design. Emergent care processes during the COVID-19 pandemic are largely influenced by other hospitals in similar medical administration areas. The second limitation is that only a small sample size was used.

Conclusion

The time delay in reperfusion therapy increased during the with-COVID-19 period compared with the pre-COVID-19 period. However, DTN time and DTP time decreased as time elapsed in the with-COVID-19 period. With the adjustment of reperfusion therapy workflows to PCS, reperfusion therapy may adapt in the era of the COVID-19 pandemic. Recently, international multi-center studies on stroke in the COVID-19 era have been reported[30, 31], and an international multi-center study on the time delay of reperfusion therapy during each phase of the COVID-19 pandemic is expected.

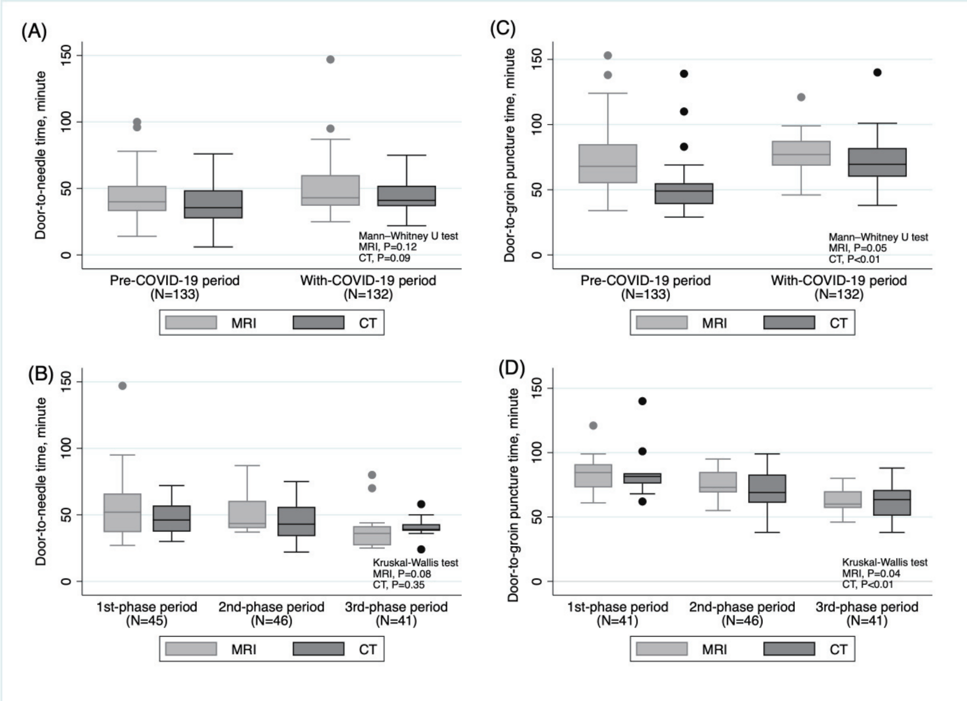

Fig. 7. Change in door-to-needle time and door-to-groin puncture time with each first-used imaging modality

Change in door-to-needle time (A and B) and door-to-groin puncture time (C and D) between the pre-COVID-19 and between each phase of the with-COVID-19 period.
Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; MRI, magnetic resonance imaging.

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Declarations

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Conflicts of Interests

Not applicable.

Availability of Data and Material

Patients' data are available upon request.

Code Availability

Not applicable.

Authors' Contributions

TY analyzed the data and wrote the manuscript. MS and JK collected the data. KT supervised the manuscript. All authors contributed to the article and approved the final version of the manuscript.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the institutional review board of the NCVC (approval number: M23-073-4). The NCVC Stroke Registry is registered at ClinicalTrials.gov (NCT02251665).

Consent to Participate/Consent for Publication

Written informed consent to undergo reperfusion therapy was obtained from each patient (or a relative if the patient had communication difficulties), and the opt-out method was used for patient recruitment.

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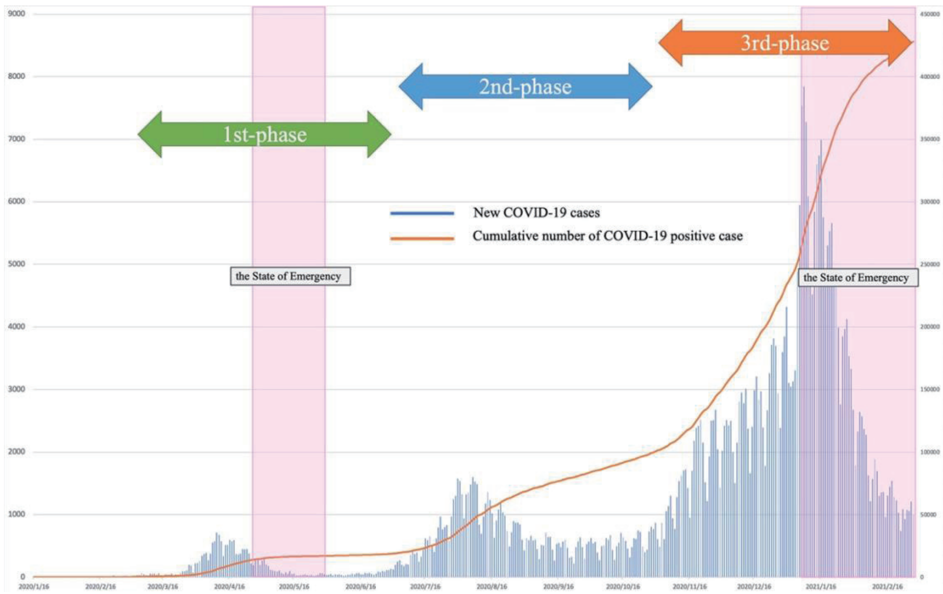

Supplemental Fig. 1. Number of patients with COVID-19 in Japan (January 16, 2020 to February 28, 2021)

A state of emergency was declared on April 7th, 2020. This was lifted on May 25th, 2020, and re-declared on January 7th, 2021, due to the third phase of the pandemic.
Edited based on openly available data from the Ministry of Health, Labour and Welfare, Japan < https://www.mhlw.go.jp/stf/covid-19/open-data.html, in Japanese > Abbreviations: COVID-19, coronavirus disease 2019.