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Original Article

Impact on Clinical Outcomes of Changes in the Practice of Mechanical Thrombectomy due to the COVID-19 Pandemic

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Objective: To evaluate whether changes in the practice of mechanical thrombectomy could affect the clinical outcomes during the coronavirus disease (COVID-19) pandemic.

Methods: Patients who underwent mechanical thrombectomy from April 2019 to March 2021 for anterior circulation proximal large artery occlusion in our institute were divided into two groups of pre- and post-COVID-19, with April 2020 assumed to be the start of the COVID-19 era with the first declaration of a state of emergency. We compared patient characteristics, proportions of patient selection depending on rapid processing of perfusion and diffusion (RAPID) CT perfusion, outcomes including treatment variables such as time and reperfusion status, and patient independence at 3 months.

Results: Data for 112 patients (median age, 79 years; 44 females) were included in the analysis. A total of 50 patients were assigned to the pre-COVID-19 group (45%). More patients were selected with RAPID CT perfusion in the post-COVID-19 compared with the pre-COVID-19 (69% vs. 16%; P <0.001). Treatment details and clinical outcomes did not differ between the groups, including the door-to-puncture time (median [interquartile range], 66 [54–90] min vs. 74 [61–89] min; P = 0.15), proportions of significant reperfusion (82% vs. 87%; P = 0.60), and modified Rankin scale score of ≤2 at 3 months (46% vs. 45%; P >0.99). Multivariate logistic regression analysis for the clinical outcome of modified Rankin scale score of ≤2 at 3 months was performed and included the following factors: age, sex, the onset-to-door time, significant reperfusion, and pre- and post-COVID-19. The treatment period did not influence the outcomes (post-COVID-19 group, odds ratio, 0.79; 95% confidence interval, 0.34–1.85, P = 0.59).

Conclusion: In the setting of a limited access to emergency MRI during the COVID-19 pandemic, RAPID CT perfusion was performed significantly more often. Changes in the practice of mechanical thrombectomy with the protected code stroke did not bring the different level of treatment and clinical outcomes as before.

Keywords ▶ mechanical thrombectomy, rapid processing of perfusion and diffusion, CT, coronavirus disease

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Introduction

Patients with acute proximal large artery occlusion in the anterior circulation are eligible for mechanical thrombectomy.[1)] This procedure is indicated depending on the time from symptom onset and various imaging and clinical mismatches.[2–4)] Salvageable brain tissue and ischemic core can be assessed with CT or MRI data automatically processed with rapid processing of perfusion and diffusion (RAPID; RapidAI, Menlo Park, CA, USA), which is a software program written in C++ programming language used to measure infarct volume.[5,6)]

During the coronavirus disease (COVID-19) pandemic, from 2020, access to various health-care systems became restricted. With regard to stroke care, the indication for

emergency MRI was carefully determined from the perspective of preventing the spread of infection.[7] In our hospital, before the pandemic, the indication for mechanical thrombectomy was primarily determined via RAPID MRI; however, due to the spread of COVID-19, we were obliged to change to RAPID CT perfusion. It was undetermined whether the change in the imaging modality affected the patient selection and outcomes of mechanical thrombectomy.

The purpose of the present study was to evaluate whether the appropriate patient selection for mechanical thrombectomy could be achieved during the COVID-19 pandemic.

Materials and Methods

The data supporting the findings of this study are available from the corresponding author on reasonable request.

Patient inclusion and exclusion criteria

All patients with acute ischemic stroke admitted to our institute within 7 days from symptom onset or the last-known-well date were prospectively enrolled in our stroke registry.[8] Data of patients enrolled from April 2019 to March 2021 were retrospectively reviewed, and those who underwent mechanical thrombectomy for anterior circulation proximal large artery occlusion were included in this study. The occlusion sites included the internal carotid artery (ICA) or the M1/M2 segments of the middle cerebral artery. We excluded patients in whom significant recanalization was achieved without any intervention, although groin puncture was performed.

Mechanical thrombectomy details

All procedures were performed by neurointerventionalists certified by the Japanese Society for Neuroendovascular Therapy according to the Guidelines for Mechanical Thrombectomy in Japan.[9] All the patients admitted within the estimation of 24 hours of last known well were determined for mechanical thrombectomy with RAPID MRI or RAPID CT perfusion, except for showing the large ischemic core on the plain CT/MRI or severe prestroke disability. The procedural goal was set to achieve extended thrombolysis in cerebral infarction (eTICI) scale ≥2b as early as possible.[1,10,11] In the post-COVID-19 group, we performed all the procedures with full personal protection equipment.

Ethical issues

An ethical standards committee approved the protocol of the registry.[8] Written informed consent for each patient was waived because we used clinical information obtained in routine clinical practice and did not impose any additional invasive procedures or costs on the patients, and the information was sufficiently anonymized.

Data collection

The following clinical patient data were collected: age, sex, smoking status, atrial fibrillation, vascular risk factors (hypertension, diabetes mellitus, and dyslipidemia), past medical history (malignancy and previous stroke or transient ischemic attack), baseline National Institutes of Health Stroke Scale score, and onset-to-door time. Outcome data were also analyzed and included proportions of the RAPID CT perfusion, procedure times (door to image and puncture, and puncture to reperfusion), proportions of first pass effect,[12] significant reperfusion of eTICI score of 2b or 2c or more, and achievement of modified Rankin scale score of ≤0–2 at 3 months after stroke onset.

Statistical analysis

The data were summarized as median (interquartile range [IQR]) for continuous variables and as frequencies and percentages for categorical variables. Patients were divided into two groups—the pre-COVID-19 group (April 2019 to April 2020) and the post-COVID-19 group (May 2020 to March 2021)—depending on whether their procedure took place before or during COVID-19, with April 2020 assumed to be the start of the COVID-19 era with the first declaration of a state of emergency. Statistical differences were assessed using the Mann–Whitney U test or Fisher's exact test, as appropriate. Explanatory variables for multivariate logistic regression models were limited to <10% of patients in the less frequent category.[13] The threshold for statistical significance was P <0.05. All statistical analyses were performed with EZR version 1.55 (Saitama Medical Center, Jichi Medical University, Saitama, Japan).[14]

Results

Data for 112 patients (median [IQR] age, 79 [71–83] years; 44 females [39%]) were analyzed (**Fig. 1**). A total of 50 patients were assigned to the pre-COVID-19 group (45%). Mechanical thrombectomy was performed in 62% (50 out of 81) and 64% (62 out of 97) of ICA/M1 occlusions in the pre- and post-COVID-19 phases, respectively (P = 0.88). Patient characteristics are shown in **Table 1**. Dyslipidemia

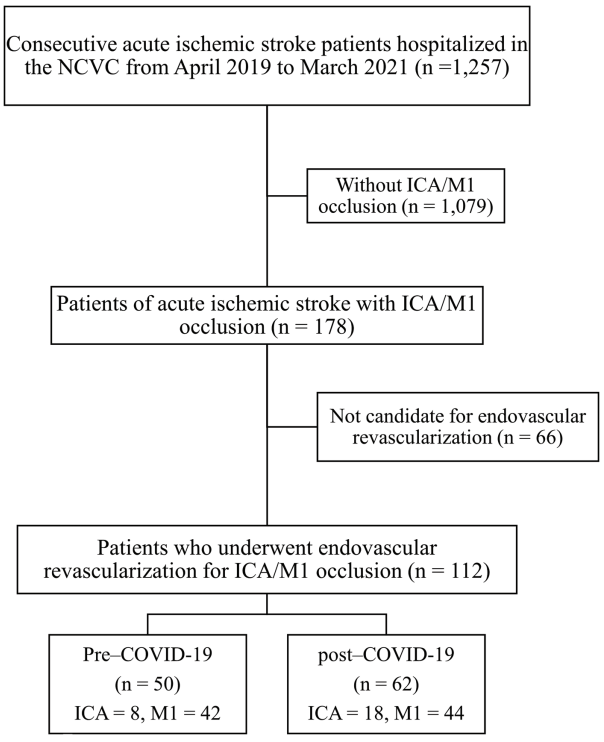

Fig. 1 Study flowchart. COVID-19: coronavirus disease; ICA: internal carotid artery; NCVC: National Cerebral and Cardiovascular Center

Table 1 Patient characteristics

	Pre (n = 50)	Post (n = 62)	*P* value
RAPID CT perfusion	8 (16)	43 (69)	<0.001*
Age (years)	79 (71–83)	78 (69–84)	0.88
Sex (female)	23 (46)	21 (34)	0.24
Premorbid mRS	0 (0–3)	0 (0–1)	0.082
NIHSS scores on admission	19 (10–25)	19 (12–24)	0.78
Onset to door (min)	105 (51–341)	85 (45–203)	0.59
ICA occlusion	8 (16)	18 (29)	0.12
Atrial fibrillation	32 (64)	40 (65)	>0.99
Hypertension	39 (78)	42 (68)	0.29
Diabetes mellitus	11 (22)	12 (19)	0.82
Smoking	21 (42)	26 (42)	>0.99
Dyslipidemia	28 (56)	21 (34)	0.034*
Malignancy	5 (10)	2 (3.2)	0.045*
Previous stroke or TIA	14 (28)	8 (13)	0.059

Asterisks indicate statistically significant difference. Data are presented as median (IQR) or number (percent). ICA: internal carotid artery; IQR: interquartile range; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale; RAPID: rapid processing of perfusion and diffusion; TIA: transient ischemic attack

(56% vs. 34%; $P = 0.034$) and malignancy (10% vs. 3.2%; $P = 0.045$) were more often found in the pre-COVID-19 group, and other factors were similar in both groups.

Table 2 Treatment and clinical outcomes

	Pre (n = 50)	Post (n = 62)	*P* value
RAPID CT perfusion, n (%)	8 (16)	43 (69)	<0.001*
Door to image (min)	26 (20–31)	25 (20–33)	0.94
Door to puncture (min)	66 (54–90)	74 (61–89)	0.15
Puncture to reperfusion (min)	60 (30–106)	40 (27–74)	0.094
First pass effect	11 (22)	27 (44)	0.027*
Significant reperfusion (eTICI 2b or more)	41 (82)	54 (87)	0.60
Significant reperfusion (eTICI 2c or more)	25 (50)	33 (53)	0.85
mRS score of ≤2 at 3 months	23 (46)	28 (45)	>0.99

Asterisks indicate statistically significant difference. Data are presented as median (IQR) or number (percent). eTICI: extended thrombolysis in cerebral infarction; IQR: interquartile range; mRS: modified Rankin scale; RAPID: rapid processing of perfusion and diffusion

Table 3 Multivariate logistic regression analysis of the post-COVID-19 group for the clinical outcome of modified Rankin scale score of ≤2 at 3 months

	Odds ratio (95% confidence interval)	*P* value
Age (years)	0.93 (0.89–0.97)	<0.001
Sex (female)	0.86 (0.35–2.11)	0.73
Onset to door (min)	0.998 (0.996–1.00)	0.069
eTICI 2b or more	4.2 (0.96–18)	0.057
Post-COVID-19 group	0.79 (0.34–1.85)	0.59

COVID-19: coronavirus disease; eTICI: extended thrombolysis in cerebral infarction

The comparison of treatment and clinical outcomes between the groups is shown in **Table 2**. More patients were selected with RAPID CT perfusion in the post-COVID-19 group (16% vs. 69%; $P < 0.001$). The door-to-puncture time did not change (median [IQR], 66 [54–90] min vs. 74 [61–89] min; $P = 0.15$), and similar reperfusion status (eTICI 2b or more, 82% vs. 87%; $P = 0.60$) and modified Rankin scale score of ≤2 at 3 months (46% vs. 45%; $P > 0.99$) were achieved in the post-COVID-19 group.

We performed a multivariate logistic regression analysis for the clinical outcome of modified Rankin scale score of ≤2 at 3 months for the influences of the COVID-19 pandemic. We included the following factors: age, sex, onset-to-door time, and significant reperfusion (eTICI score of 2b or more) (**Table 3**). The COVID-19 pandemic did not significantly influence the outcomes (post-COVID-19 group, odds ratio, 0.79; 95% confidence interval, 0.34–1.85, $P = 0.59$).

Discussion

In this study, we showed that treatment and clinical outcomes of mechanical thrombectomy did not differ depending on the treatment periods before and after the COVID-19 pandemic.

Under ordinary circumstances, the onset time should be estimated by comparing diffusion-weighted images (DWI) and FLAIR on MRI to determine the indication for therapy with intravenous recombinant tissue plasminogen activator and mechanical thrombectomy.[9] According to the protected code stroke, Japanese Stroke Society PCS Working Group,[7] MRI should not be performed in confirmed or suspected COVID-19 cases and full personal protection equipment is required for the examination of undetermined or confirmed COVID-19 patients, from the perspective of infection control. However, it is desirable to determine the indications for mechanical thrombectomy based on the current guideline even in confirmed or suspected COVID-19 cases in view of its high efficacy and the potential social loss in case mechanical thrombectomy is not performed. Therefore, to select patient eligible for mechanical thrombectomy during the COVID-19 pandemic, it is preferred to use CT-based imaging consistent with the current guidelines. Our study showed that mechanical thrombectomy with full personal protection equipment did not bring a significant treatment delay. The similar door-to-imaging time between pre- and post-COVID-19 groups might reflect the stability of our emergency imaging studies.

Because DWI of MRI can assess cellular edema in acute stroke, apparent diffusion coefficient $<620 \times 10^{-3}$ mm^2/s is depicted and converted as ischemic core in the RAPID protocol.[5] In the case of CT perfusion, only regions with blood flow abnormalities can be identified; however, a relation with tissue fate seems to be present. On the basis of studies comparing CT perfusion findings with DWI, an ischemic core on CT perfusion at a threshold of <30% of the opposite side corresponded well with an acute DWI lesion.[15] As shown in our present study, patient selection for mechanical thrombectomy based on RAPID CT perfusion under the COVID-19 pandemic is valid.

The prevalence of RAPID in Japan is limited, and it is necessary to consider patient selection without perfusion images in general hospitals. In the 6- to 24-h time frame from the last-known-well date, the clinical and core mismatch of patients with Alberta Stroke Program Early CT Score (ASPECTS) of 6–10 was 80% associated with the judgement of the criteria described in the DAWN (The DWI or CT Perfusion Assessment with Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention with Trevo) trial.[16] Therefore, it is reasonable to determine the indication depending on patient's ASPECTS of 6–10 even in cases of 6- to 24-h time frame if no perfusion image is available, especially in the era of the COVID-19 pandemic.[17]

Limitations

This study had several limitations. First, the imaging modality was determined by each patient's physician, which might have caused some selection bias. Second, the present study included data from a single center and the sample size was relatively small. More cases with RAPID CT may bring a different conclusion. Further evaluation in multiple centers is desirable to validate the findings of this study.

Conclusion

In the setting of a limited access to emergency MRI during the COVID-19 pandemic, RAPID CT perfusion was performed significantly more often. Changes in the practice of mechanical thrombectomy with the protected code stroke did not bring the different level of treatment and clinical outcomes as before.

Disclosure Statement

Koji Iihara received a fund for endowed courses from Idorsia Pharmaceuticals Japan. Tetsu Satow received a research grant from CANON Medical Systems Corporation. Masatoshi Koga received a research grant from Daiichi Sankyo Company, Limited. All the other authors have no conflicts of interest.

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