



Predictive Value of Acute Neurological Progression Using Bayesian CT Perfusion for Acute Ischemic Stroke with Large or Median Vessel Occlusion

Shinya Yoshii, Satoshi Fujita, Yu Hiramoto, Morito Hayashi, and Satoshi Iwabuchi

Objective: Since the efficacy of mechanical thrombectomy (MT) for acute cerebral infarction due to large vessel occlusion has been proven, the time available for treatment has gradually increased. Currently, under certain conditions, treatment is indicated up to 24 h from onset. Based on neurological signs and imaging diagnosis, Stroke Treatment Guideline 2021 recommends initiation of MT within 6–24 h from onset. Herein, we retrospectively investigated the relationship between cerebral perfusion imaging evaluation and prognosis in patients with acute cerebral infarction due to large or median vessel occlusion.

Methods: Fifty-one patients diagnosed with acute cerebral infarction due to large or median vessel occlusions in anterior circulation between November 2019 and December 2021 were divided into medical care and reconstructive therapy (including tissue plasminogen activator [t-PA] therapy and MT) groups. The primary outcome was changes in the National Institutes of Health Stroke Scale (NIHSS) at admission and 1 week after onset. Patients in the medical care group were divided into those whose NIHSS did not worsen and those whose NIHSS worsened. Those in the reconstructive therapy group were divided into those whose NIHSS improved and those whose NIHSS did not improve. We evaluated the relationship between improvement factors in acute neurological symptoms and penumbral and core volumes from computed tomography perfusion performed at admission.

Results: Of 45 eligible patients, 10 received medical care without t-PA or MT and 35 underwent reconstructive therapy, including t-PA and MT. Among the 10 patients in the medical care group, 3 had worsening symptoms and 7 did not. The mean and median (interquartile range [IQR]) penumbra volumes were significantly higher in patients with worsening symptoms than in those without. The receiver operating characteristic (ROC) curve showed a threshold value of 28.6 mL with an area under the curve (AUC) of 0.952. Among the 35 patients in the reconstructive therapy group, symptoms improved for 29 but did not improve for 6. The mean and median (IQR) core volumes were significantly higher in patients whose symptoms did not improve than in those whose symptoms improved. The ROC curve showed a threshold value of 25 mL and an AUC of 0.632.

Conclusion: Evaluation of penumbra volumes could detect cases with worsening symptoms in cases where medical care was performed, and evaluation of core volumes may detect cases with non-improved symptoms in cases that received reconstructive therapy.

Keywords ► acute ischemic stroke, mechanical thrombectomy, penumbra volume, acute neurological progression

Department of Neurosurgery, Toho University Ohashi Medical Center, Tokyo, Japan

Received: July 24, 2023; Accepted: October 24, 2023
Corresponding author: Satoshi Fujita. Department of Neurosurgery, Toho University Ohashi Medical Center, 2-22-36 Ohashi, Meguro-ku, Tokyo 153-8515, Japan
Email: satoshi.fujita@med.toho-u.ac.jp



This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives International License.

©2024 The Japanese Society for Neuroendovascular Therapy

Introduction

In recent years, mechanical thrombectomy (MT) for acute ischemic stroke (AIS) due to large vessel occlusion has become a common treatment, gradually increasing the time available for treatment. Under certain conditions, treatment is considered to be up to 24 h after onset. According to the Stroke Guidelines 2021, initiating MT for AIS of the internal carotid artery or middle cerebral artery (M1) 6–24 h after onset based on neurological signs and imaging diagnosis is

reasonable. However, we have encountered cases where medical care treatment was selected based on symptoms and imaging. The symptoms progressed in cases where extensive hemorrhagic infarction occurred even after MT was administered early from the onset. In 2019, we evaluated patients with CT perfusion (Vitrea Workstation; Canon Medical Systems, Otawara, Japan) using the Bayesian method, a robust probabilistic method that minimizes the effects of oscillation, tracer delay, and high levels of noise during residue function estimation compared with other deconvolution methods¹⁾; however, there are little data on Vitrea, and treatment criteria or evidences such as RAPID (iSchema View, Menlo Park, CA, USA) have not been established. In our hospital, CT perfusion imaging is aggressively performed from early onset, and treatment strategies are formulated using the penumbra and core volumes obtained from computed tomography perfusion (CTP). This study retrospectively examined the relationship between penumbra and core volumes and the progression of acute neurological symptoms in patients with AIS due to large or median vessel occlusion.

Materials and Methods

Patients were retrospectively evaluated from November 2019 to December 2021 at Toho University Medical Center for acute cerebral infarction due to anterior circulation obstruction detected within 24 h of onset using a CT scanner (Aquilion ONE; Canon Medical Systems). Automated perfusion analyzer software (Vitrea Workstation; Canon Medical Systems) was also used to assess cerebral circulation, cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time to peak (TTP). The criteria for selecting patients in our study were as follows: 1) ≥ 18 years old, 2) admission to the hospital within 24 h of onset, 3) core volume at an upper limit of 130 mL, and 4) AIS due to occlusion of the large or median vessels of the anterior circulation (the common carotid, internal carotid, and M1–M3 portion of the middle cerebral arteries). Tandem occlusion of the extracranial internal carotid artery and the M1 and M2 segments of the middle cerebral artery were included. The Ethics Committee of Toho University Medical Center approved this study (approval number: H21013).

Imaging protocol and analysis

CTP data were collected as a series of 22 volumes using the Neuro ONE protocol. The device used was Aquilion ONE GENESIS Edition (Canon Medical Systems) with a slice thickness of 0.5 mm and 320 slices. The contrast agent used

was Iopamidol Syringe 370 (Teva Takeda Pharma Ltd., Nagoya, Japan) with 50 mL injected at a rate of 5 mL/s and then flushed with saline solution. Images were captured with intermittent continuous scans at 2-s intervals from 5 to 36 s and continuous scans at 5-s intervals from 40 to 65 s. The imaging parameters included 1 s scan, tube voltage of 80 kV peak, and standard deviation 5 (SD5) at 0.5-mm image thickness with auto exposure control, and the dose was a minimum of 10 mA and a maximum of 120 mA. The maximum CT dose index for a volume scan was 4.2. Vitrea (version 8.3; Canon Medical Systems) was used as the analysis software.

Vitrea detects infarct as tissue with relative CBV $< 38\%$ compared to healthy brain tissue and penumbra as tissue with 5.3 s increase in TTP.

Graphic: a case presentation of CT perfusion and MRI

Reference cases of CTA and CTP performed simultaneously using MRI and Vitrea are shown in **Fig. 1**. Diffusion-weighted MRI (DWI) revealed a slightly high-intensity area in the right hemisphere (**Fig. 1A**). MRA showed occlusion of the right middle cerebral artery M2 (**Fig. 1B**). In the Vitrea, CTA revealed occlusion of the right middle cerebral artery M2 (**Fig. 1C**). The core area indicated a 38% reduction in CBV compared to the contralateral side (**Fig. 1E**), and the penumbra area indicated a 5.3-s delay in TTP compared to the contralateral side (**Fig. 1F**).

Outcomes

The primary outcome was the change in the National Institutes of Health Stroke Scale (NIHSS) score at admission and 1 week after onset. In the medical care group, patients without worsening of the NIHSS score were defined as non-deteriorating cases and those with worsening of the NIHSS score were defined as deteriorating cases. In the reconstructive therapy group, patients were classified as improved if their NIHSS score improved by ≥ 5 points and as non-improved if their NIHSS score improved by < 5 points or did not improve from admission. The secondary outcome was the percentage of patients with a modified Rankin scale (mRS) of 0–2 after 90 days.

Statistical analysis

All statistical analyses were performed using EZR software (Version 1.55). The non-paired t-test was used for between-group comparisons of means, and the Mann–Whitney test was used for between-group comparisons of medians, with $p < 0.05$ indicating a significant difference.

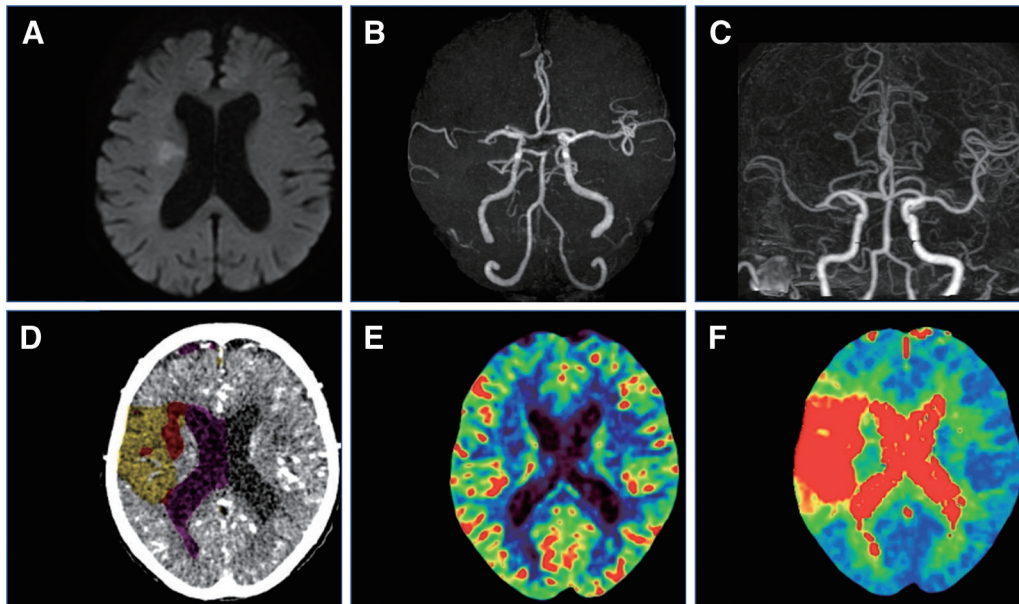


Fig. 1 Analysis of head MRI/MRA and Bayesian CT perfusion. (A) Head DWI image showing a high-intensity area around the right lateral ventricle. (B) Head MRA image showing occlusion of the right middle cerebral artery M2. (C) CTA image of the head showing occlusion of the right middle cerebral artery M2. (D) Vitrea summary map showing the ischemic core volume as a red area and the ischemic penumbra volume as a yellow area. (E) CBV with decreased blood flow in 38% of the ischemic core region is shown in blue around the right ventricle. (F) TTP with the ischemic penumbra region in the right cerebral hemisphere is shown in red, indicating an area of delayed TTP contrast compared to the contralateral side at 5.3 s. CBV: cerebral blood volume; DWI: diffusion-weighted MRI; TTP: time to peak

Clinical and demographic data were presented as mean (SD) or median (interquartile range [IQR]), as appropriate. Receiver operating characteristic (ROC) curve analysis was used to calculate the best cutoff time-point for the penumbral core volume.

Results

Patients' characteristics

The study evaluated 51 patients with AIS due to large or median vessel occlusion using Vitrea imaging (**Fig. 2**). One patient was discharged within 1 week; therefore, follow-up data were unavailable. Two patients underwent angiography; however, angiography was attempted because of the strong tortuosity. One patient had a subarachnoid hemorrhage due to perforation during MT. Two patients had a core (>130 mL). The baseline characteristics are shown in **Table 1**. Median age and pre-mRS scores did not change. At admission, the median (IQR) NIHSS score was 5 (1.5–9.25) for the medical care group and 18 (8–21) for the reconstructive therapy group. The median penumbra volume was 21.3 mL (1.98–35.4 mL) for the medical care group and 78.8 mL (28.99–104.34 mL) for the reconstructive therapy group. Core volumes were higher in the reconstructive therapy group than those in the medical group,

with a median (IQR) of 8.4 mL (3.01–19.38 mL) and 0.86 mL (0.33–1.645 mL), respectively.

Outcomes

Penumbra volume, core volume, and penumbra to core ratio (P/C) values were compared among 10 medical care treatment group patients. The mean penumbra volume was 12.4 ± 14.7 mL, and the median (IQR) was 3.6 mL (1.08–21.33 mL) in non-deteriorating cases; however, in three patients with deteriorating cases, the mean was 35.5 ± 6.2 mL, and the median (IQR) was 37.9 mL (33.23–39.05 mL), significantly higher than non-deteriorating cases ($p = 0.03$). Analysis using the ROC curve showed a threshold value of 28.6 mL and an area under the curve (AUC) of 0.952 (**Fig. 3A**). The mean core volume was 4.10 ± 8.66 mL, and the median (IQR) was 1.04 mL (0.23–1.69 mL) in nondeteriorating cases. The three patients with deteriorating cases had no difference, with a mean of 0.99 ± 0.71 mL and a median (IQR) of 0.672 mL (0.58–1.24 mL) ($p = 1$). Analysis using the ROC curve showed a threshold value of 1.81 mL and an AUC of 0.476 (**Fig. 3B**). The mean P/C value was 10.2 ± 11.1 , with a median (IQR) of 10.6 (2.30–11.59) in nondeteriorating cases; however, the three patients with deteriorating cases had a mean of 50.8 ± 31.5 and a median (IQR) of 59.8 (37.8–68.2), significantly higher than those in nondeteriorating

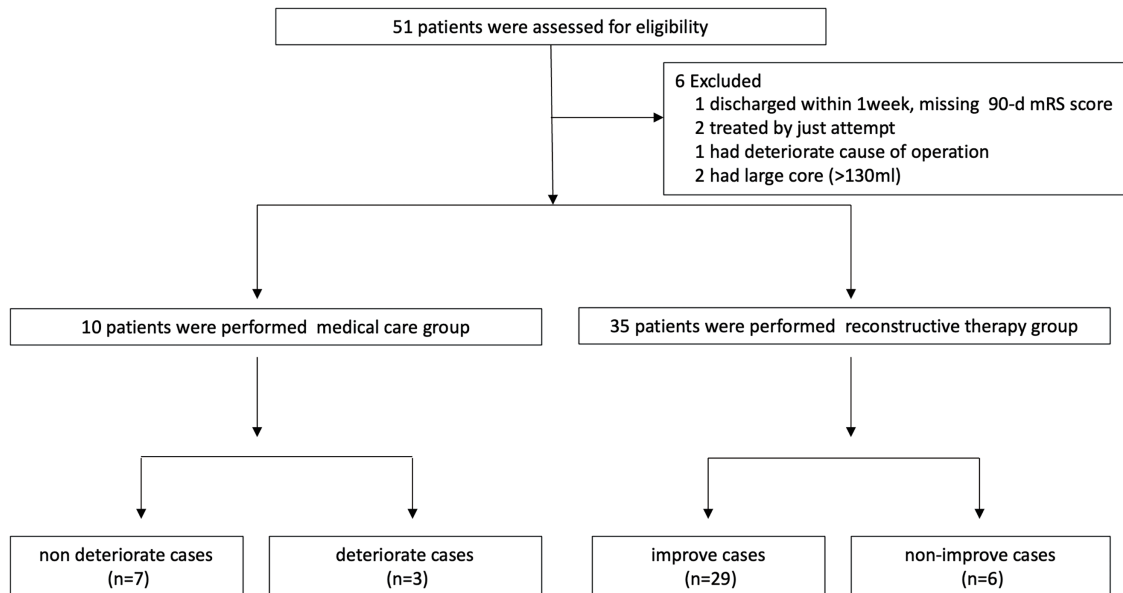


Fig. 2 Fifty-one patients were evaluated using Vitrea. One patient was discharged voluntarily within a week and could not be followed up; two patients underwent angioplasty but the attempted procedure was halted, due to severe vascular tortuosity; one suffered from vascular perforation during thrombectomy; and two patients with a high core volume (>130 mL) were excluded. The patients were divided into two groups: 10 patients who were followed up conservatively and 35 who underwent reconstructive therapy, including t-PA and MT. The NIHSS scores at the onset and 1 week later were compared. Seven patients in the medical care group did not have worsening symptoms as in the nondeteriorating cases; in contrast, three patients had worsening symptoms as in the deteriorating cases. In the reconstructive therapy group, 29 patients improved and six patients did not. MT: mechanical thrombectomy; NIHSS: National Institutes of Health Stroke Scale; t-PA: tissue plasminogen activator

Table 1 Clinical characteristics of the patients

	Medical care group n = 10	Reconstructive therapy group n = 35
Median age	77 (62.5–86.25)	79 (69–82.5)
Male	4 (40%)	18 (51%)
Median pre-mRS (IQR)	0 (0–1.5)	0 (0–0)
Median NIHSS (IQR)	5 (1.5–9.25)	18 (8–21)
Low NIHSS (<6 points) case	6 (60%)	8 (23%)
Occlusion site		
CCA, ICA	1	4
M1	2	16
M2-3	6	12
Tandem ICA-M1	1	3
Median ASPECTS (IQR)	10 (10–10)	10 (8–10)
Median penumbra volume (IQR)	21.3 (1.98–35.4)	78.8 (28.99–104.34)
Median core volume (IQR)	0.86 (0.33–1.645)	8.4 (3.01–19.38)
Median penumbra/core (IQR)	11.6 (5.51–28.44)	7.8 (4.44–12.94)
Onset unknown case	3 (30%)	9 (25.7%)
MT	NA	27 (77.1%)
Median time O2D (IQR)	55 (40–56)	60 (40–76.75)
Median time O2I (IQR)	92 (64.5–269.5)	77 (62–105.25)
Median time O2P (IQR)	NA	159 (125–210)
Median time O2R (IQR)	NA	209 (173–273)
TICI grade >2b	NA	24/27 (88.9%)
Intravenous rt-PA use	NA	16 (45.7%)

ASPECTS: Alberta Stroke Program Early CT Score; CCA: common carotid artery; ICA: internal carotid artery; IQR: interquartile range; mRS: modified Rankin scale; MT: mechanical thrombectomy; NIHSS: National Institutes of Health Stroke Scale; O2D: onset to door; O2I: onset to image; O2P: onset to puncture; O2R: onset to recanalization; rt-PA: recombinant tissue plasminogen activator; TICI: thrombolysis in cerebral infarction

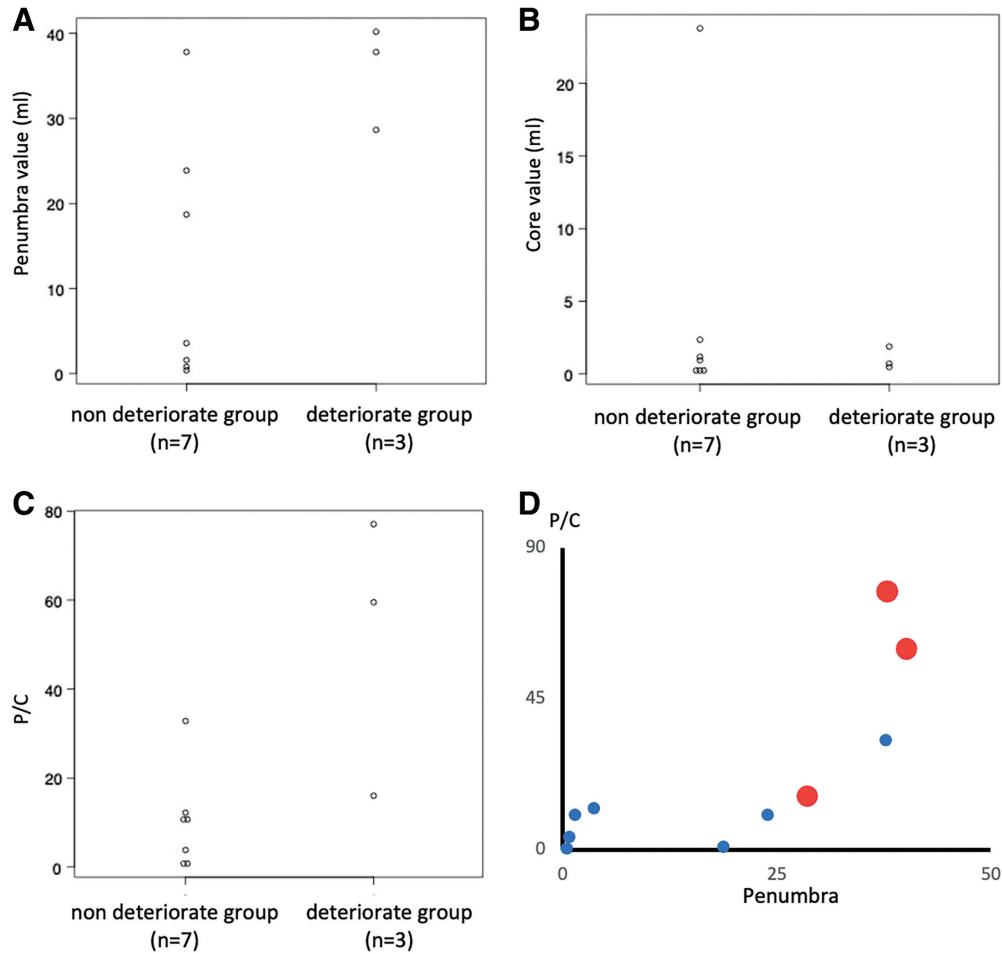


Fig. 3 The medical care group analysis (10 cases) is shown as a dot plot. **(A)** Penumbra volume: In nondeteriorating cases, the mean volume was 12.4 ± 14.7 mL and the median (IQR) was 3.6 mL (1.08–21.33 mL), and in deteriorating cases, the mean volume was 35.5 ± 6.2 mL and the median (IQR) was 37.9 mL (33.23–39.05 mL) ($p = 0.03$). The threshold volume was 28.6 mL, and AUC was 0.952. **(B)** Core volume: In nondeteriorating cases, the mean volume was 4.10 ± 8.66 mL and the median (IQR) was 1.04 mL (0.23–1.69 mL). There was no difference in deteriorating cases, with a mean of 0.99 ± 0.71 mL and a median (IQR) of 0.672 mL (0.58–1.24 mL) ($p = 1$). The threshold volume was 1.81 mL and AUC was 0.476. **(C)** penumbra to core ratio (P/C) values: A mean of 10.2 ± 11.1 and a median (IQR) of 10.6 (2.30–11.59) were observed in nondeteriorating cases. For patients with deteriorating cases, the mean was 50.8 ± 31.5 and the median (IQR) was 59.8 (37.8–68.2) ($p = 0.03$). The threshold value was 15.8 and AUC was 0.952. **(D)** P/C value and penumbra volume in the medical care group are shown in a dot plot. The vertical axis is the P/C value, and the horizontal axis is the penumbra volume. Red dots indicate deteriorating cases, and blue dots indicate nondeteriorating cases. AUC: area under the curve; IQR: interquartile range

cases ($p = 0.03$). The threshold was 15.8 with an AUC of 0.952 (**Fig. 3C**). The P/C value and penumbra volumes in the medical care group are shown as dotted plots. Red dots indicate deteriorating cases, and blue dots indicate nondeteriorating cases (**Fig. 3D**). It was found that cases with high P/C and penumbra volumes >28.6 mL tended to deteriorate. The secondary outcome, the percentage of patients with mRS 0–2 at 90 days, was significantly higher in the non-deteriorating cases ($p = 0.01$): 6 (85.7%) in the nondeteriorating cases and 0 (0%) in the deteriorating cases.

The penumbra volume, core volume, and P/C values were compared in 35 patients in the reconstructive therapy

group. The mean penumbra volume was 71.19 ± 43.45 mL, and the median (IQR) was 78.41 mL (28.46–103.84 mL) in improved cases; however, six patients with nonimproved cases had a mean penumbra volume of 85.86 ± 62.75 mL and a median (IQR) of 82.12 mL (44.61–107.09 mL), with no difference in the two groups ($p = 0.68$). Analysis using the ROC curve showed a threshold value of 78.8 mL and an AUC of 0.557 (**Fig. 4A**). The mean core volume was 14.4 ± 19.5 mL, and the median (IQR) was 8.4 mL (2.88–18.36 mL) in improved cases. The mean core volume of the six patients in the nonimproved cases tended to be higher than that in the improved cases, with a mean of 21.8 ± 20.5 mL

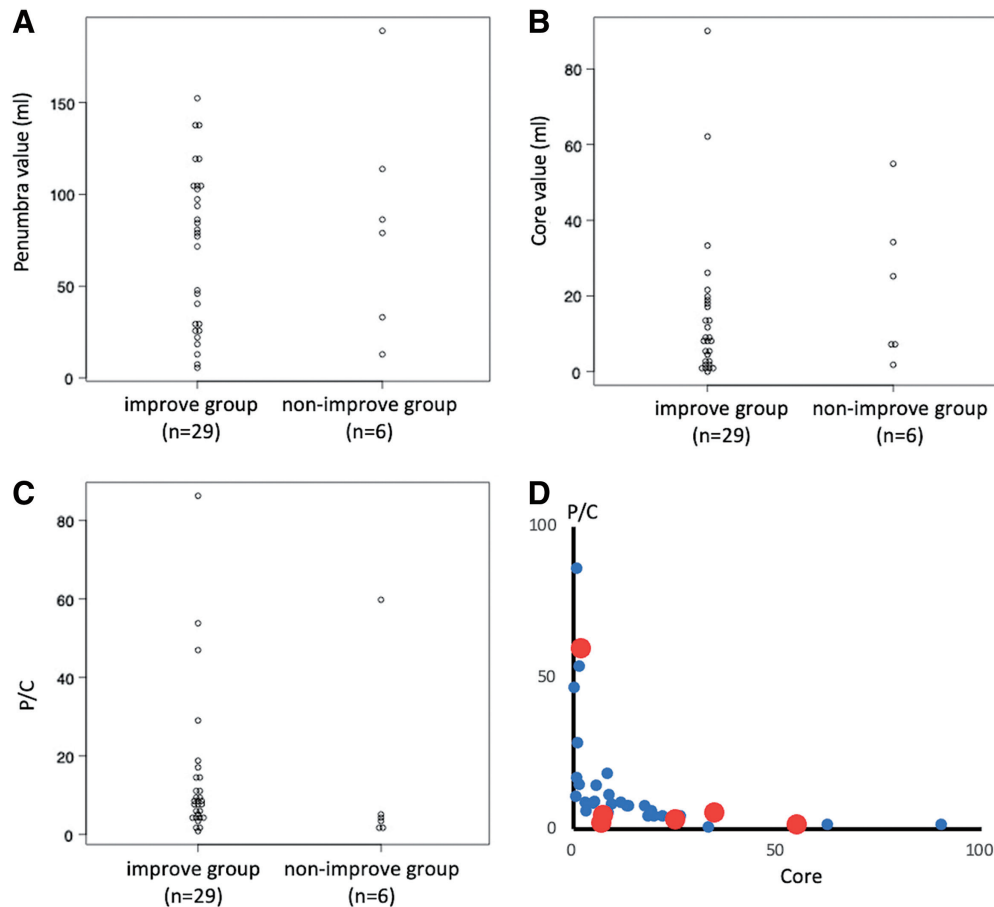


Fig. 4 Dot plot showing the analysis of the reconstructive therapy group (35 cases). **(A)** Penumbra volume: In the improved group, the mean volume was 71.19 ± 43.45 mL and the median (IQR) was 78.41 mL (28.46–103.84 mL), and in the nonimproved group, the mean volume was 85.86 ± 62.75 mL and the median (IQR) was 82.12 mL (44.61–107.09 mL) ($p = 0.68$). The threshold volume was 78.8 mL and AUC was 0.557. **(B)** Core volume: In the improved group, the mean volume was 14.4 ± 19.5 mL and the median (IQR) was 8.4 mL (2.88–18.36 mL). In the nonimproved group, the mean was 21.8 ± 20.5 mL and the median (IQR) was 16.2 mL (6.98–32.22 mL) ($p = 0.33$). The threshold volume was 25 mL and AUC was 0.632. **(C)** penumbra to core ratio (P/C) values: The mean was 14.3 ± 18.5 and the median (IQR) was 8.5 (4.56–14.52) for patients in the improved group, and the mean was 12.8 ± 23.1 and the median (IQR) was 3.8 (2.26–5.24) ($p = 0.11$) for patients in the nonimproved group. The threshold value was 5.5 and AUC was 0.713. **(D)** P/C value and core volume in the reconstructive therapy group are shown in a dot plot. The vertical axis is the P/C value, and the horizontal axis is the penumbra volume. Red dots indicate nonimproved cases, and blue dots indicate improved cases. AUC: area under the curve; IQR: interquartile range

and a median (IQR) of 16.2 mL (6.98–32.22 mL) ($p = 0.33$). ROC curve analysis showed a threshold value of 25 mL and an AUC of 0.632 (**Fig. 4B**). The mean P/C value was 14.3 ± 18.5 , and the median (IQR) was 8.5 (4.56–14.52) in improved cases; however, the six patients in the nonimproved cases had a mean of 12.8 ± 23.1 and a median (IQR) of 3.8 (2.26–5.24), which were lower than those in the improved cases ($p = 0.11$). The threshold was 5.5 with an AUC of 0.713 (**Fig. 4C**). The P/C value and penumbra volumes in the reconstructive therapy group are shown as dot plots. Red and blue dots indicate nonimproved and improved cases, respectively (**Fig. 4D**). It was found that cases with low P/C and core volumes >25 mL tended to be nonimproved cases. The secondary outcome, the percentage

of patients with mRS 0–2 at 90 days, was significantly higher in the improved cases ($p = 0.03$): 16 (55.2%) in the improved cases and one (16.7%) in the nonimproved cases.

Case presentation

A 73-year-old woman presented to our hospital with a chief complaint of dysrhythmia. Her symptoms improved when she visited our hospital, with an NIHSS score of 0. Head CT showed no obvious abnormality (**Fig. 5A**), but CTA showed occlusion in the right M2–3, and CTP showed abnormal perfusion in the right parietal cortex. CBV was decreased, TTP was prolonged, and the summary map showed a penumbra volume of 40.21 mL, a core volume of 0.672 mL, and a P/C value of 59.84 (**Fig. 5B**). As there were

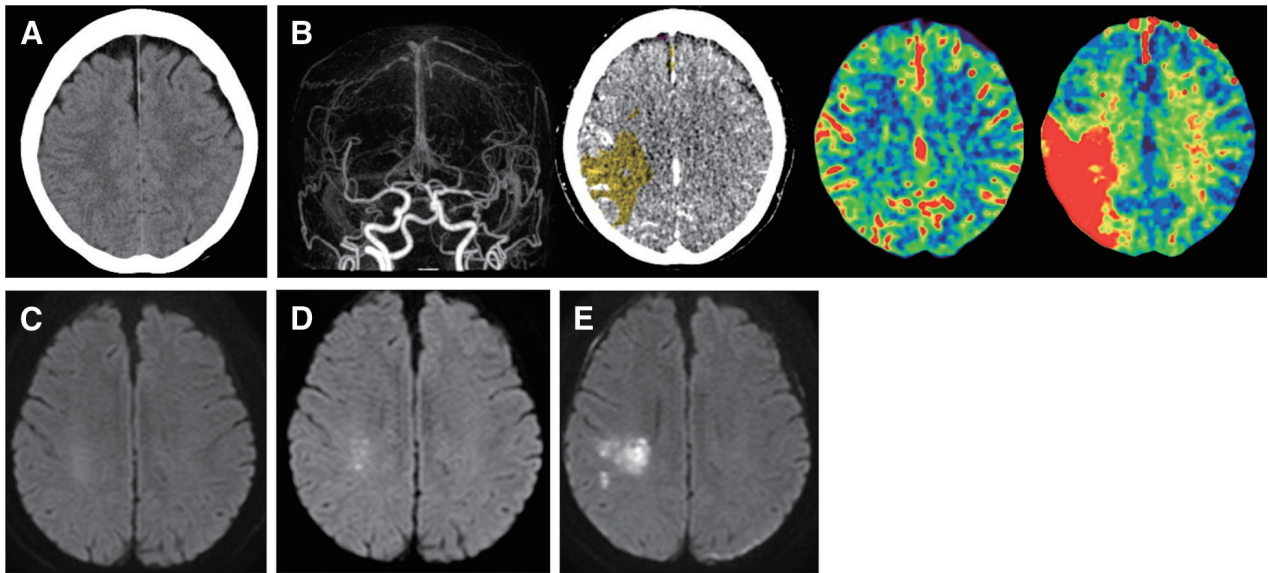


Fig. 5 A 73-year-old woman presented with a chief complaint of dysrhythmia. **(A)** CT scan of the head showing no obvious abnormal findings. **(B)** CTA on arrival showing occlusion of M3 in the right middle cerebral artery, CTP in the head, and suspected ischemic changes in the right parietal lobe, with decreased CBV and CBF and prolonged TTP and MTT. The penumbra to core ratio (P/C) value was 59.84.

(C) DWI at the time of admission showing no abnormal signal area. **(D)** DWI of the head 1 day after admission showing a high-intensity area. **(E)** DWI of the head 6 days after admission showing a clear high-intensity area with an enlarged ischemic cerebral lesion. CBF: cerebral blood flow; CBV: cerebral blood volume; CTP: computed tomography perfusion; DWI: diffusion-weighted MRI; MTT: mean transit time

no symptoms, the patient was treated conservatively. Head DWI performed simultaneously showed no high-intensity areas (**Fig. 5C**). However, the following day, the left sensory disturbance progressed, and head DWI revealed a high-intensity area in the right parietal lobe (**Fig. 5D**). Six days later, head DWI showed an enlarged infarct area (**Fig. 5E**), the NIHSS score worsened to 5 points, and the patient was transferred to a rehabilitation hospital.

Discussion

We evaluated the images of patients with AIS due to large or median vessel occlusion using Vitrea, a Bayesian CTP. In our study, even in patients with mild symptoms who did not require reconstructive therapy, such as tissue plasminogen activator (t-PA) or MT, a penumbra volume of 28.6 mL was considered a threshold value above which the ischemic extent may increase and reconstructive therapy should be considered. In the reconstructive therapy group, CTP values did not differ significantly between the improved and non-improved cases. It has been reported that the Bayesian method, which is a feature of the Vitrea, allows a more accurate evaluation of the core volume than the conventional singular value decomposition method used in RAPID.^{1,2} Furthermore, Vitrea has been reported to be more accurate in assessing penumbra volume than other software methods, such as Sphere and RAPID, suggesting

that Vitrea is noninferior to RAPID.^{3,4} It is reported that the evaluation of CBV and MTT as parameters of CTP using Vitrea can predict the final volume range of cerebral infarction after recanalization of the AIS.⁵ Recently, the validity of CTP has been investigated in cases where evidence still needs to be established, such as low NIHSS scores and large-core, mild cases. In cases of late time window stroke and unknown onset, DAWN⁶ and Diffuse3⁷ reported that MT is effective even if the treatment time is extended. Recently, using CTP, it was reported that for AIS caused by large vessel occlusion in Japanese patients with onset within 24 h, no difference was observed in prognosis between patients with an early time window (≤ 6 h from onset) and those with a late time window (6–24 h from onset).⁸ The investigators reported that the infarct growth velocity was slower in late time window cases, which was related to the expansion of the infarct area.

Regarding early time window cases, it was reported that the core volume evaluated by CTP was overestimated compared to the final core volume evaluated using Definition AS Siemens.⁹ CTP overestimates the core volume in patients in the early time window, particularly in those with poor collateral circulation.¹⁰ It has also been reported that CTP is unnecessary in early time window cases because there is no significant difference in the time to treatment between groups with and without CTP, and the safety and prognosis at 3 months are the same.¹¹ Based on the above,

there may be no reason to use CTP in early time window cases actively.

We often encounter mild cases with low NIHSS scores that make it difficult to decide to perform reconstructive therapy. MT in patients with low NIHSS scores (NIHSS <6) may worsen neurological abnormalities within 24 h, but the outcome at 3 months is not different from that in patients who did not receive MT.¹²⁾ Similarly, Sarraj et al. reported an increased risk of bleeding with MT in mild stroke (NIHSS <6) when compared with other therapies; however, there was no increase in the good prognosis group, making the use of MT in mild cases skeptical.¹³⁾ However, we have encountered cases in which patients deteriorated after conservative treatment and cases in which aggressive reconstructive treatment led to worsening symptoms due to bleeding and other complications. In this study, we found that the penumbra volume was higher in patients with acute progression of neurological symptoms than in those with no progression of symptoms and low NIHSS scores. In addition, the medical treatment group had a significantly worse mRS score at 90 days in patients with acute progressive symptoms, suggesting the need for further consideration of reconstructive treatment in patients with low NIHSS scores.

Patients with large core volumes are generally considered at a high risk of bleeding and are not indicated for MT. It has been reported that a lower CBV is associated with a risk of hemorrhagic infarction.¹⁴⁾ The RAPID treatment criteria often recommend MT for core volumes of <70 mL. The RESCUE-Japan LIMIT trial reported that MT was more effective than conservative treatment in cases of extensive ischemic core volume with an Alberta Stroke Program Early CT Score (ASPECTS) of 3–5 points.¹⁵⁾ However, this study did not use CTP because 80% of the patients underwent preoperative head MRI. In this study, we reported that CTP may be effective if a safer treatment strategy is developed. Similarly, it has been reported that the core volume with the highest benefit from MT is 70–100 mL, with an increased risk of hemorrhagic infarction above the upper limit of 120 mL using RAPID.¹⁶⁾ Another study reported less benefit from MT when the patient was over 76 years of age and when the core volume was >90 mL.¹⁷⁾ This study excluded two cases with core volumes of >130 mL. One of the two patients was not treated with MT because his CTP was at 200 mL core volume, despite a CT-ASPECTS score of 8 within 2 h of onset. We believe that fatal hemorrhagic complications could have been avoided. This suggests that even if the time from onset to treatment is short and the ASPECTS score is high, CTP can detect high-risk cases and

make treatment safer. On the other hand, while some studies report that CTP is unnecessary,^{18,19)} some papers report the effectiveness of image evaluation using artificial inter-agency,^{20,21)} and we await further reports to determine the indications for MT. Few studies have examined the use of penumbra volume assessed by CTP concerning therapeutic indications for MT. However, choosing conservative treatment for patients who do not progress is important in terms of healthcare economics and medical staff strength. The reason for the difference in prognosis between the improved and nonimproved cases was not related to CTP data, but to the fact that the non-improved cases had more left lesions and more passes for thrombectomy. In the nonimproved cases, left lesions accounted for 66%, while it was 53% in the improved cases. Furthermore, the average number of passes for thrombectomy in the non-improved cases was 4.2, while in the improved cases, it was 1.2.

Limitations

This study had some limitations. The first was the small number of patients. Although we could process the data statistically, the number of patients in the medical care group with worsening symptoms was low. Previously, various institutions have reported the use of limits on core volumes; however, in this study, the number of cases was not large enough to set an upper limit. Hence, high-core-volume cases were used as the exclusion criteria. Second, this retrospective study may have led to treatment bias, especially because it included patients with pre-mRS4. Therefore, a prospective multicenter study with stricter inclusion criteria is necessary.

Conclusion

We evaluated the relationship between the penumbra and core volume and the progression of acute neurological symptoms in patients with a low NIHSS score; CTP on admission indicated that a penumbra volume of 28.6 mL or higher was a threshold for worsening symptoms and that reconstructive therapy such as t-PA or MT should be considered. In the reconstructive therapy group, a core volume of 25 mL or higher may not improve acute neurological symptoms. We believe that using Bayesian CT perfusion, the choice of reconstructive or medical treatment for AIS should be investigated.

Disclosure Statement

All authors have no conflict of interest.

References

- 1) Sakai Y, Delman BN, Fifi JT, et al. Estimation of ischemic core volume using computed tomographic perfusion. *Stroke* 2018; 49: 2345–2352.
- 2) Kudo K, Boutelier T, Pautot F, et al. Bayesian analysis of perfusion-weighted imaging to predict infarct volume: comparison with singular value decomposition. *Magn Reson Med Sci* 2014; 13: 45–50.
- 3) Rava RA, Snyder K, Mokin M, et al. Assessment of computed tomography perfusion software in predicting spatial location and volume of infarct in acute ischemic stroke patients: a comparison of Sphere, Vitrea, and RAPID. *J Neurointerv Surg* 2021; 13: 130–135.
- 4) Rava RA, Snyder KV, Mokin M, et al. Assessment of a Bayesian Vitrea CT perfusion analysis to predict final infarct and penumbra volumes in patients with acute ischemic stroke: a comparison with RAPID. *AJNR Am J Neuroradiol* 2020; 41: 206–212.
- 5) Hirai S, Sato H, Yamamura T, et al. Correlation between the CT perfusion parameter values and response to recanalization in patients with acute ischemic stroke. *J Neuroendovasc Ther* 2022; 16: 577–585.
- 6) Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018; 378: 11–21.
- 7) Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med* 2018; 378: 708–718.
- 8) Inoue M, Yoshimoto T, Toyoda K, et al. Mechanical thrombectomy up to 24 hours in large vessel occlusions and infarct velocity assessment. *J Am Heart Assoc* 2021; 10: e022880.
- 9) Boned S, Padroni M, Rubiera M, et al. Admission CT perfusion may overestimate initial infarct core: the ghost infarct core concept. *J Neurointerv Surg* 2017; 9: 66–69.
- 10) García-Tornel Á, Campos D, Rubiera M, et al. Ischemic core overestimation on computed tomography perfusion. *Stroke* 2021; 52: 1751–1760.
- 11) Jadhav AP, Goyal M, Ospel J, et al. Thrombectomy with and without computed tomography perfusion imaging in the early time window: a pooled analysis of patient-level data. *Stroke* 2022; 53: 1348–1353.
- 12) Volny O, Zerna C, Tomek A, et al. Thrombectomy vs medical management in low NIHSS acute anterior circulation stroke. *Neurology* 2020; 95: e3364–e3372.
- 13) Sarraj A, Hassan A, Savitz SI, et al. Endovascular thrombectomy for mild strokes: how low should we go? *Stroke* 2018; 49: 2398–2405.
- 14) Jain AR, Jain M, Kanthala AR, et al. Association of CT perfusion parameters with hemorrhagic transformation in acute ischemic stroke. *AJNR Am J Neuroradiol* 2013; 34: 1895–1900.
- 15) Yoshimura S, Sakai N, Yamagami H, et al. Endovascular therapy for acute stroke with a large ischemic region. *N Engl J Med* 2022; 386: 1303–1313.
- 16) Yoshimoto T, Inoue M, Tanaka K, et al. Identifying large ischemic core volume ranges in acute stroke that can benefit from mechanical thrombectomy. *J Neurointerv Surg* 2021; 13: 1081–1087.
- 17) Yang H, Lin D, Lin X, et al. Outcomes and CT perfusion thresholds of mechanical thrombectomy for patients with large ischemic core lesions. *Front Neurol* 2022; 13: 856403.
- 18) Nannoni S, Ricciardi F, Strambo D, et al. Correlation between ASPECTS and core volume on CT perfusion: impact of time since stroke onset and presence of large-vessel occlusion. *AJNR Am J Neuroradiol* 2021; 42: 422–428.
- 19) Nguyen TN, Abdalkader M, Nagel S, et al. Noncontrast computed tomography vs computed tomography perfusion or magnetic resonance imaging selection in late presentation of stroke with large-vessel occlusion. *JAMA Neurol* 2022; 79: 22–31.
- 20) Kuang H, Najm M, Chakraborty D, et al. Automated ASPECTS on noncontrast CT scans in patients with acute ischemic stroke using machine learning. *AJNR Am J Neuroradiol* 2019; 40: 33–38.
- 21) Sundaram VK, Goldstein J, Wheelwright D, et al. Automated ASPECTS in acute ischemic stroke: a comparative analysis with CT perfusion. *AJNR Am J Neuroradiol* 2019; 40: 2033–2038.