Hyperperfusion after Endovascular Reperfusion Therapy for Acute Ischemic Stroke

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Background and purpose: Patients with acute ischemic stroke (AIS) may display prolonged neurological deficits and conscious disturbance even after successful endovascular thrombectomy. We hypothesized that hemodynamic change after reperfusion might influence outcomes. This study investigated the factors causing hyperperfusion and outcomes. *Methods*: We retrospectively analyzed 27 patients with AIS who underwent successful acute revascularization (TICI: Thrombolysis in Cerebral Infarction 2b + 3). Changes of the neurological status were precisely assessed by using the National Institutes of Health Stroke Scale (NIHSS). Ischemic lesions were scored by MRI with diffusion-weighted imaging (DWI), and blood flow in the middle cerebral artery territory was assessed by MRI with arterial spin labeling. Univariate analysis was performed to investigate correlations between hyperperfusion and demographic factors or the functional prognosis. *Results*: Thirteen of the 27 (48%) patients developed hyperperfusion after reperfusion. A significant correlation was seen between hyperperfusion and the improvement of NIHSS at 24 hours ($P < .0001$), the duration of disturbance of consciousness (days) ($P < .0001$), DWI-ASPECTS ($P = .001$), hemorrhagic transformation ($P = .007$), and mRS less than or equal to 2 at 90 days ($P = .007$). *Conclusions*: The present findings suggested that some patients with AIS will develop hyperperfusion after successful acute revascularization. The status of hyperperfusion could prolong conscious disturbance and affect outcomes. Since the mechanism of hyperperfusion after revascularization depends on stroke etiology, diagnosing the type of ischemic stroke in the acute stage is important for managing postoperative treatment.

Key Words: Acute ischemic stroke—arterial spin labeling—hyperperfusion

Introduction

The recent development of a neurointerventional device has led to marked improvement of endovascular thrombectomy for acute ischemic stroke (AIS). Current large-scale studies have suggested that endovascular thrombectomy can achieve a good outcome (mRS ≤ 2) in selected patients if performed in less than 16 or less than 24 hours after the onset of stroke.[1] Goyal et al reviewed large cohort studies of patients with AIS[2] and suggested that about 50% of patients may achieve a good outcome (mRS ≤ 2). However current study showed that ischemic reperfusion injury could be considered.[3] Actually some AIS patients clinically show prolonged conscious disturbance after successful acute revascularization, despite having a

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small lesion of permanent brain damage on imaging, but the pathophysiology underlying this discrepancy remains unclear. Interestingly, recent hemodynamic studies have demonstrated that hyperperfusion can cause impairment of cognitive function after vascular reconstruction surgery.[4] One possible mechanism to explain this clinical discrepancy might be differences of blood flow recovery after revascularization. In patients with carotid artery stenosis undergoing carotid endarterectomy or carotid artery stenting, cerebral hyperperfusion syndrome is a well-known phenomenon,[5,6] as a result of cerebral hyperpefusion. Cerebral hyperperfusion syndrome is defined as an increase of cerebral blood flow (CBF) that exceeds the brain tissue demand and causes a neurological deficit. We hypothesized that some patients with AIS might develop similar reperfusion problems. Therefore, we retrospectively investigated hemodynamic changes in AIS patients together with detailed consecutive assessment of their neurological findings.

Methods

The authorized local ethical committee approved this retrospective study and the requirement for informed consent was waived. Between April 2016 and March 2018, 70 patients with AIS were treated at our hospital and 50 patients successfully achieved Thrombolysis in Cererbral Infarction (TICI) 2b + 3. Of these 50 patients, 27 patients underwent MRI before and after treatment. Postoperative MRI underwent within 24 hours after treatment. A total of these 27 patients were included in this retrospective study. The neurological status was evaluated by the NIHSS (preoperatively and 24 hours postoperatively), and an early dramatic response to treatment was defined as a decrease of the NIHSS score by greater than or equal to 8 from baseline or an NIHSS score of 0-2 at 24 hours. Stroke etiology was classified according to the Trial of Org 10172 in Acute Stroke Treatment criteria[7] as large artery atherosclerosis (LAA) or cardioembolism (CE). Disturbance of consciousness was defined as somnolence, stupor, lethargy, or coma. The duration of disturbance of consciousness (in days) was evaluated.

The extent of cerebral infarction before and after treatment was assessed by using diffusion-weighted imaging-ASPECTS (DWI-ASPECTS) MRI. Small lesion was defined as DWI-ASPECTS greater than over equal to 7, and we analyzed the correlation between small lesion and the duration of consciousness, outcome especially in cerebral hyperperfusion group.

In addition, MRI with arterial spin labeling (ASL) was performed just before treatment and within 24 hours after it. Postoperative hyperperfusion was defined as patchy areas with visually perceivable increased CBF on ASL maps either within or around the corresponding lesion observed on DWI images when compared with the homologous contralateral hemisphere.[8] Serial imaging studies were performed until neurological recovery. Hemorrhagic transformation were assessed by T2*-weighted image, according to the Second European-Australasian Acute Stroke Study (ECASS II) criteria.[9]

Imaging Protocol

All patients underwent consecutive imaging by using a 1.5 TMR scanner (Signa Explorer; GE Healthcare Ltd., Tokyo, Japan) equipped with an 8-channel head coil. The protocol included DWI, TOF-MRA, T2* and ASL with the post-labeling delay set at 1.525 ms. The total scanning time was 8 minutes per examination.

Statistical Analysis

Mean values were determined and the standard error of the mean (SE, $\sigma/\sqrt{n}$) was calculated as an estimate of the population mean. To compare differences between 2 groups, Fisher's exact test was employed for categorical variables and the Mann-Whitney *U*-test was used for quantitative variables. The level of significance was set at $\alpha < .05$. Statistical analyses were carried out with the JMP statistical package (JMP version 13, SAS Institute, Inc., Cary, North Carolina).

Results

Patient Demographic Profile

The 27 patients included 14 men and 13 women (mean age: 78 years, range: 68-91 years). Their demographic profile is summarized in Table 1. All patients received endovascular recanalization was successful (TICI = 2b in 3 patients and TICI = 3 in 24 patients). The site of occlusion was the internal carotid artery (ICA) in 12 patients and the middle cerebral artery (MCA) in 15 patients. The mean preoperative DWI-ASPECTS score was 7.7 points (range: 3-11). The 21 patients (78%) observed small lesion (DWI-ASPECTS $\geqq$ 7). The mean time from onset to reperfusion was 363 minutes (range: 116-1740 minutes). Hemorrhagic transformation was observed in 8 patients (30%).

Thirteen patients developed hyperperfusion after revascularization and all patients showed no improvement of NIHSS at 24 hours after therapy. There was a significant correlation between hyperperfusion and the following parameters (hyperperfusion group versus nonhyperperfusion group): improvement of NIHSS at 24 hours (0 versus 11 $P < .0001$), the duration of disturbance of consciousness (mean: 7.7 versus 0.6 $P < .0001$), DWI-ASPECTS (mean: 6.5 versus 8.9; $P = .001$), hemorrhagic transformation (7 versus 1; $P = .007$) and mRS less than or equal to 2 at 90 days (2 versus 9; $P = .007$). There was a positive association between hyperperfusion and the time from onset to reperfusion (mean: 502 versus 235; $P = .08$). In patients with hyperperfusion, 8 of 13 patients (62%) had small lesion. The correlation with the duration of disturbance of consciousness was significantly short in small lesion (mean 4.9 days versus 10.3 days; $P = .01$). However, there were no relationship between

Table 1. *Summary of hyperperfusion after acute revascularization*

	Total (n = 27)	Hyperperfuion (+) (n = 13 48%)	Hyperperfusion (−) (n = 14 52%)	*P* value
Age, mean ± SE	78 ± 1.4	78 ± 2.3	79 ± 1.6	.69
Female, n (%)	13 (48)	6 (46)	7 (50)	.84
NIHSS, mean ± SE	19 ± 1.5	18 ± 1.8	21 ± 2.3	.55
Improve of NIHSS at 24 h	11 (55)	0 (0)	11 (85)	<.0001
DWI-ASPECTS, mean ± SE	7.7 ± .4	6.5 ± .5	8.9 ± .4	.001
ICA, n (%)	12 (44)	7 (54)	5 (36)	.34
Duration of disturbance of consciousness, mean ± SE (d)	4.0 ± .9	7.7 ± 1.0	.6 ± .7	<.0001
O2R, mean ± SE (min)	363 ± 72	502 ± 141	235 ± 15	.08
Hemorrhagic trasnformation, n (%)	8 (30)	7 (54)	1 (13)	.007
mRS (90 d) ≦2, n (%)	11 (41)	2 (15)	9 (64)	.007

Abbreviations: ICA, internal cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; O2R, onset to reperfusion.

lesion and outcome: mRS less than or equal to 2 at 90 days. Two patients with small lesion achieved mRS less than or equal to 2 at 90 days.

Etiology

Large Artery Atherosclerosis

Six of the 27 patients had AIS due to large artery occlusion (ICA or MCA) and hyperperfusion was detected in 4 of these 6 patients (67%). Their demographic profile is summarized in Table 2. Among the patients with hyperperfusion, none showed improvement of NIHSS at 24 hours and only one had a good outcome at 90 days. The mean DWI-ASPECTS score was 1 point lower in the patients with hyperperfusion than in those without hyperperfusion (7 versus 8 points), and the time from onset to reperfusion was longer in patients with hyperperfusion than in those without hyperperfusion (1045 versus 275 minutes).

Cardioembolism

Twenty-one of the 27 patients had AIS due to CE and hyperperfusion was detected in 9 of these 21 patients (43%). Their demographic profile is summarized in Table 3. Among the patients with hyperperfusion, none showed improvement of NIHSS after 24 hours and only 1 patient showed good outcome at 90 days. The mean DWI-ASPECTS score was 5.9 points lower in the patients with hyperperfusion than in those without hyperperfusion (P = .001), but the time from onset to reperfusion was almost the same in the patients with and without hyperperfusion (260 versus 227 minutes).

Representative Cases

Case 1

An 82-year-old man with a history of atrial fibrillation developed right hemiparesis, aphasia. His NIHSS was 27 on admission (onset-to-door time: 51 minutes). MRI revealed a hyperdense area in the left MCA territory (DWI-ASPECTS 5) (Fig 1). Thrombectomy using a stent retriever achieved recanalization (TICI = 3) at about 207 minutes after the onset. Neurological findings showed no improvement at 24 hours after reperfusion (NIHSS 27). ASL revealed hyperperfusion in the ischemic area from the day after surgery to 7 days after (Fig 2). Following the

Table 2. *Summary of hyperperfusion after acute revascularization (large artery atherosclerosis)*

	Total (n = 6)	Hyperperfuion (+) (n = 4 67%)	Hyperperfuion (−) (n = 2 33%)
Age, mean ± SE	74 ± 2.0	73 ± 2.6	78 ± .5
Female, n (%)	1 (17)	1 (25)	0 (0)
NIHSS, mean ± SE	16 ± 3.1	15 ± 4.8	19 ± 1.0
Improve of NIHSS at 24 h	2 (33)	0 (0)	2 (100)
DWI-ASPECTS, mean ± SE	7 ± .5	7 ± .8	8 ± .5
ICA, n (%)	5 (83)	3 (75)	2 (100)
Duration of disturbance of consciousness, mean ± SE (d)	4.2 ± 1.5	6.0 ± 1.6	.5 ± .5
O2R, mean ± SE (min)	788 ± 265	1045 ± 332	275 ± 3.5
Hemorrhagic trasnformation, n (%)	0 (0)	0 (0)	0 (0)
mRS (90 d) ≤2, n (%)	3 (50)	1 (25)	2 (100)

Abbreviations: ICA, internal cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; O2R, onset to reperfusion.

Table 3. *Summary of hyperperfusion after acute revascularization (cardioembolic)*

	Total (n = 21)	Hyperperfuion (+) (n = 9 43%)	Hyperperfuion (−) (n = 12 57%)	*P* value
Age, mean ± SE	79 ± 1.6	80 ± 2.8	79 ± 1.9	.8
Female, n (%)	12 (57)	5 (56)	7 (58)	.8
NIHSS, mean ± SE	21 ± 1.7	20 ± 1.6	21 ± 2.7	.69
Improve of NIHSS at 24 h	9 (42)	0 (0)	9 (75)	.0006
DWI-ASPECTS, mean ± SE	7.7 ± .5	5.9 ± .6	9.1 ± .4	.001
ICA, n (%)	7 (33)	4 (44)	3 (25)	.35
Duration of disturbance of consciousness, mean ± SE (d)	4 ± 1.0	8.4 ± 1.3	.6 ± .2	<.0001
O2R, mean ± SE (min)	241 ± 15	260 ± 28	227 ± 17	.49
Hemorrhagic trasnformation, n (%)	8 (38)	7 (88)	1 (13)	.001
mRS (90 d) ≦2, n (%)	8 (38)	1 (11)	7 (58)	.02

Abbreviations: ICA, internal cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; O2R, onset to reperfusion.

resolution of hyperperfusion, his level of consciousness improved. Right hemiparesis improved, but motor aphasia persisted at 90 days after the onset (mRS 3).

Case 2

An 80-year-old man with a history of hypertension experienced apraxia on the day before AIS, followed by the sudden onset of conjugate deviation and right-sided paralysis with motor aphasia. His NIHSS was 24 on admission (onset-to-door time: 1105 minutes). MRI revealed left ICA occlusion and a hyperdense area in the left MCA territory (DWI-ASPECTS 7). Digital subtraction angiography (DSA) showed occlusion of the ipsilateral ICA by atherosclerotic plaque was diagnosed (Fig 3). Transluminal balloon plasty was performed with proximal protection and a stent was deployed, resulting in complete recanalization (TICI = 3) about 1459 minutes after the onset. Neurological findings showed no improvement at 24 hours after reperfusion. (NIHSS 29). ASL demonstrated hyperperfusion of the ischemic area from the day after therapy to 7 days afterwards (Fig 4). After hyperperfusion resolved, his level of consciousness improved. Right-sided paralysis and motor aphasia were improved at 90 days after the onset of stroke (mRS 1).

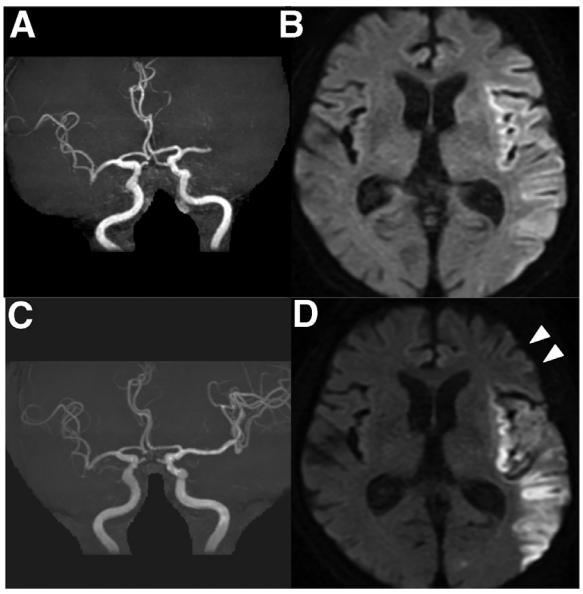

Figure 1. *An 82-year-old man with cardioembolic stroke in the left middle cerebral artery territory (A). DWI shows a high intensity area in the left middle cerebral artery territory (B). Postoperative magnetic resonance angiography demonstrates complete revascularization of the left middle cerebral artery territory (C). Postoperative DWI shows disappearance of the high signal intensity area in the left frontal lobe (arrow) (D). DWI, diffusion-weighted imaging.*

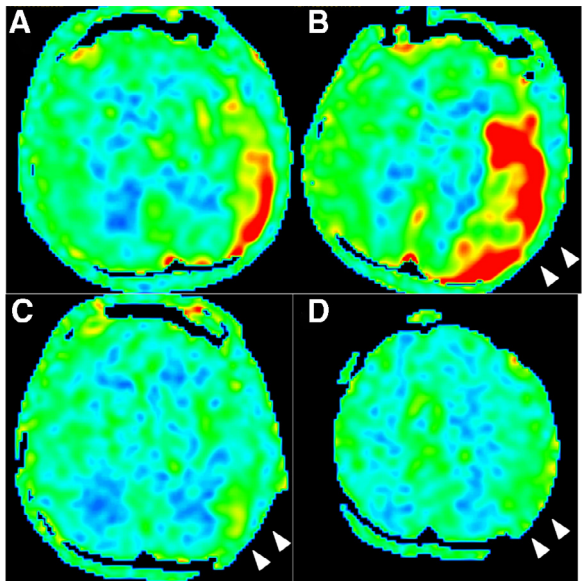

Figure 2. *Postoperative ASL shows hyperperfusion in the left middle cerebral artery territory (A). One week later, the area of hyperperfusion has expanded in the left middle cerebral artery territory (arrow) (B). Two weeks after surgery, the hyperperfusion has disappeared (arrow) (C, D). ASL, arterial spin labeling.*

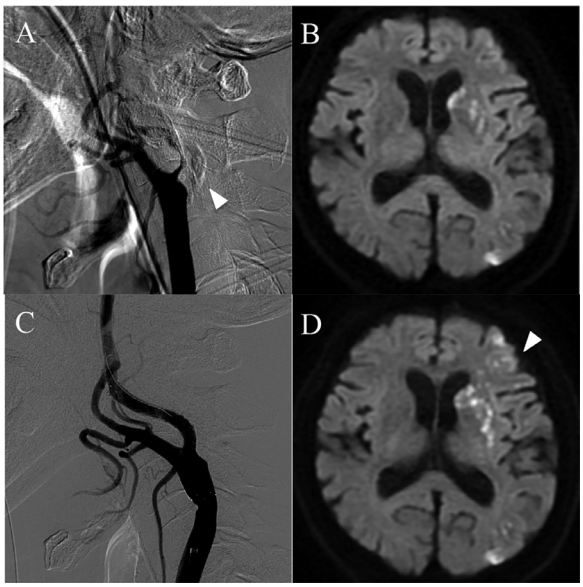

Figure 3. *An 80-year-old man with AIS due to left ICA occlusion. Preoperative DSA demonstrates ICA occlusion with calcification at the bifurcation (arrow) (A). DWI shows scattered high intensity areas in the left middle cerebral artery territory (B). Postoperative DSA displays complete revascularization of the left ICA with stenting (C). Postoperative DWI demonstrates additional high signal intensity areas in the left frontal lobe (arrow) (D). AIS, acute ischemic stroke; DSA, digital subtraction angiography; DWI, diffusion-weighted imaging; ICA, internal carotid artery.*

Discussion

The present study revealed that postoperative hyperperfusion even after successful revascularization was associated with prolonged conscious disturbance. None of the patients with hyperperfusion achieved acute neurological recovery (in 24 hours after reperfusion) and the duration of disturbance of consciousness was approximately 7 days longer. Actually some patients who presented prolonged conscious disturbance suffered from numerous complications such as pneumonia, which might associate with worse outcomes. The outcome at 90 days was not good as expected after successful reperfusion.

The incidence of hyperperfusion after mechanical thrombectomy was relatively high accounting 28% of patients who achieved TICI greater than over equal to 2b reperfusion in the presented study. Currently a few studies including case series revealed this new concept in reperfusion therapy for AIS,[8,10] therefore the actual incidence of hyperperfusion after mechanical thrombectomy remains unclear. In addition, there were 2 stroke etiologies associated with hyperperfusion. The majority of AIS in the present series was due to CE, while the minor etiology was LAA and hyperperfusion tended to occur in the latter group. The hemodynamics of these 2 stroke etiologies may differ, therefore the mechanism of hyperperfusion should be discussed separately.

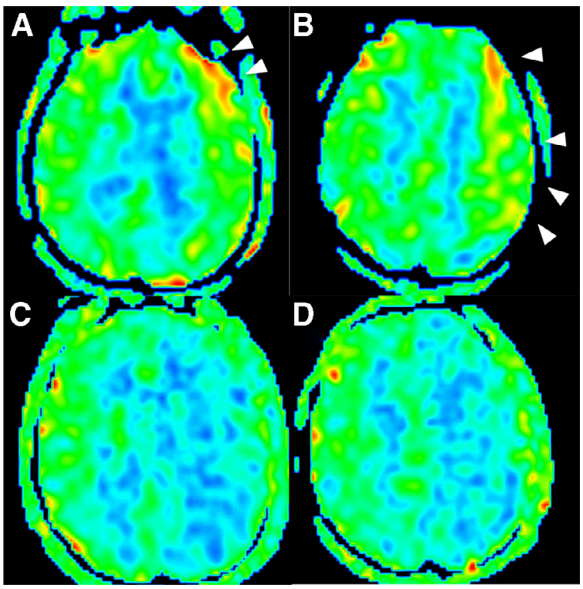

Figure 4. *Postoperative ASL shows hyperperfusion in the left middle cerebral artery territory (A and B). One week later, the area of hyperperfusion in the left middle cerebral artery territory has disappeared, and low perfusion consistent with the site of cerebral infarction is observed (C and D). ASL, arterial spin labeling.*

Large Artery Atherosclerosis

LAA was classified as AIS with atherosclerotic proximal ICA stenosis or occlusion. Chronic stenosis of a large vessel promotes the development of collateral circulation, which could be the main reason for the significant difference of DWI-ASPECTS between the patients with and without hyperperfusion. Chronic severe stenosis is associated with a high risk of hyperperfusion after revascularization, which is considered to be due to poor cerebrovascular reserve and decreased autoregulation.[11] This may explain the high frequency of hyperperfusion in patients with LAA.

Acute treatment is suggested to be a risk factor for hyperperfusion depending on the procedure in ICA stenosis,[12] and gradual expansion should be considered to avoid postoperative hyperperfusion.[13] Actually, the 2 LAA patients without hyperperfusion after the procedure were treated by percutaneous transluminal angioplasty alone. On the other hand, even if reperfusion is achieved by thrombectomy, immediate reocclusion frequently occurs in this type of acute stroke.[14] We also experienced a patient without hyperperfusion, who developed occlusion of ICA one day after treatment by percutaneous transluminal angioplasty. There is clearly no unanimity in the literature regarding the optimal strategy for the technical approach to patients with such lesions.[15] Currently, the combination of angioplasty and stent placement for proximal stenosis or occlusion is not considered useful according to the most recent American Heart Association guidelines on management of AIS.[16] Therefore, treatment of LAA patients with AIS should be performed carefully

to obtain effective outcomes and the appropriate treatment strategy will contribute to avoiding hyperperfusion.

Cardioembolism

In the group with CE, 9 out of 21 patients (43%) demonstrated hyperperfusion. Although the mean DWI-ASPECTS value was low in the patients with hyperperfusion, there was no difference of the time from onset to reperfusion between the patients with or without hyperperfusion. ASPECTS was proposed as a method for semi-quantitatively assessing early ischemic changes, with DWI-ASPECTS adding acute ischemic lesions in the cerebral white matter.[17,18] Thus, our findings suggested that the extent of acute ischemia and the absence of collateral circulation, rather than the reperfusion time, might contribute to hyperperfusion. A previous study suggested that "luxury perfusion" may indicate metabolic failure and correspond to hyperperfusion.[8] Previous physiological studies have suggested that changes of blood-brain barrier permeability occur when brain tissue is damaged by ischemia, which may increase the risk of hyperperfusion after reperfusion.[8] Liu suggested that sudden occlusion of the culprit artery and lack of collateral circulation may be the major reasons for an increase of blood-brain barrier permeability after CE.[19] The present study suggested that poor collateral circulation was associated with hyperperfusion after reperfusion therapy in CE, as was the area of early brain ischemia showing a low DWI-ASPECTS value.

Relationship between Hyperperfusion and Outcomes

Hyperperfusion after reperfusion is associated with hemorrhagic transformation and poor prognosis as well.[8,20] After bleeding occurs, the mortality rate is reported to exceed 50%.[21] Our study showed that hyperperfusion had an effect on the hemorrhagic transformation and outcome. Perioperative management centered on blood pressure control is important for preventing hyperperfusion.[21] Once patients were diagnosed harboring hyperperfusion, strict management of blood pressure under 120/80 mmHg was recommended.[22] Lower blood pressure could reduce the incidence of cerebral hyperperfusion after reperfusion therapy. Moreover to prevent hyperperfusion, propofol was recommended in the treatment hyperperfusion result to normalize CBF.[20]

It is of interest that even patients with small brain infarction (DWI-ASPECT $\geqq$ 7) could show hyperperfusion in a short period. In the presented study, 6 of 8 patients had prolonged neurological deficits presumably due to initial brain damage, whereas the rest 2 patients could show full recovery returning to community mobility. We believe that intensive care after reperfusion therapy would be necessary to obtain better clinical result, otherwise these patients with small brain infarction might suffer from reperfusion brain damage including hemorrhagic transformation.[3] To clarify risk factors of hyperperfusion and establish better clinical management, further study would be warranted.

Limitations

This study had several limitations. First, it was a retrospective case series, so the number of patients was too small for statistical evaluation. Further studies are needed to clarify the factors associated with hyperperfusion after reperfusion.

Secondly, the definition of hyperperfusion after reperfusion was evaluated qualitatively using ASL. Quantitative assessment of ASL would be preferable to find a cut-off value for hyperperfusion.

Finally, previous study suggested that CBF assessment by ASL and that by other modality (eg, SPECT or CT perfusion) had excellent correlation.[8,23] ASL could be performed repeatedly less invasively, therefore expected as first line examination to evaluate hemodynamic change after acute reperfusion therapy. However ASL tended to overestimate CBF compared with other modalities.[23] The evaluation using ASL may be related to high frequency of hyperperfusion in this study.

Conclusion

In AIS patients, CBF can change dramatically after revascularization. Hyperperfusion might be a possible pathophysiologic mechanism of prolonged conscious disturbance after reperfusion therapy, and could affect on patient outcomes. To diagnose the etiology of stroke and to detect hyperperfusion after reperfusion therapy would help postoperative management of AIS patients.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

1. 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.
2. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-1731.
3. Gauberti M, Lapergue B, Gory B, et al. Ischemia-reperfusion injury after endovascular thrombectomy for ischemic stroke. Stroke 2018;49:3071-3074.
4. Ogasawara K, Yamadate K, Kobayashi M, et al. Postoperative cerebral hyperperfusion associated with impaired cognitive function in patients undergoing carotid endarterectomy. J Neurosurg 2005;102:38-44.
5. Moulakakis KG, Mylonas SN, Sfyroeras GS, et al. Hyperperfusion syndrome after carotid revascularization. J Vasc Surg 2009;49:1060-1068.

6. van Mook WN, Rennenberg RJ, Schurink GW, et al. Cerebral hyperperfusion syndrome. Lancet Neurol 2005;4:877-888.
7. Adams Jr. HP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. Toast. Trial of org 10172 in acute stroke treatment. Stroke 1993;24:35-41.
8. Yu S, Liebeskind DS, Dua S, et al. Postischemic hyperperfusion on arterial spin labeled perfusion MRI is linked to hemorrhagic transformation in stroke. J Cereb Blood Flow Metab 2015;35:630-637.
9. Larre V, von Kummer RR, Bluhmki E, et al. Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator: a secondary analysis of the European-Australasian Acute Stroke Study (ECASS II). Stroke 2001;32:438-441.
10. Okazaki S, Yamagami H, Toyoda K, et al. Cerebral hyperperfusion on arterial spin labeling MRI after reperfusion therapy is related to hemorrhagic transformation. J Cereb Blood Flow Metab 2017;37:3087-3090.
11. Ogasawara K, Yukawa H, Kobayashi M, et al. Prediction and monitoring of cerebral hyperperfusion after carotid endarterectomy by using single-photon emission computerized tomography scanning. J Neurosurg 2003;99:504-510.
12. Maas MB, Kwolek CJ, Hirsch JA, et al. Clinical risk predictors for cerebral hyperperfusion syndrome after carotid endarterectomy. J Neurol Neurosurg Psychiatry 2013;84:569-572.
13. Yoshimura S, Kitajima H, Enomoto Y, et al. Staged angioplasty for carotid artery stenosis to prevent postoperative hyperperfusion. Neurosurgery 2009;64. 122-128; discussion 128-129.
14. Kang DH, Kim YW, Hwang YH, et al. Instant reocclusion following mechanical thrombectomy of in situ thromboocclusion and the role of low-dose intra-arterial tirofiban. Cerebrovasc Dis 2014;37:350-355.
15. Yoon W, Kim SK, Park MS, et al. Endovascular treatment and the outcomes of atherosclerotic intracranial stenosis in patients with hyperacute stroke. Neurosurgery 2015;76:680-686. discussion 686.
16. Powers WJ, Derdeyn CP, Biller J, et al. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2015;46:3020-3035.
17. Kawano H, Hirano T, Nakajima M, et al. Modified ASPECTS for DWI including deep white matter lesions predicts subsequent intracranial hemorrhage. J Neurol 2012;259:2045-2052.
18. Barber PA, Demchuk AM, Zhang J, et al. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS study group. Alberta stroke programme early CT score. Lancet 2000;355:1670-1674.
19. Liu C, Shi F, Chen Z, et al. Severe blood-brain barrier disruption in cardioembolic stroke. Front Neurol 2018;9:55.
20. Farooq MU, Goshgarian C, Gorelick PB, et al. Pathophysiology and management of reperfusion injury and hyperperfusion syndrome after carotid endarterectomy and carotid artery stenting. Exp Transl Stroke Med 2016;8:7.
21. Ogasawara K, Sakai N, Kuroiwa T, et al. Intracranial hemorrhage associated with cerebral hyperperfusion syndrome following carotid endarterectomy and carotid artery stenting: retrospective review of 4494 patients. J Neurosurg 2007;107:1130-1136.
22. Abou-Chebl A, Reginelli J, Yadav JS, et al. Intensive treatment of hypertension decreases the risk of hyperperfusion and intracerebral hemorrhage following carotid artery stenting. Catheter Cardiovasc Interv 2007;69:690-696.
23. Uchihashi Y, Hosoda K, Kohmura E, et al. Clinical application of arterial spin-labeling MR imaging in patients with carotid stenosis: quantitative comparative study with single-photon emission CT. AJNR Am J Neuroradiol 2011;32:1545-1551.