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Original Article

The Usefulness of Perfusion Magnetic Resonance Imaging with Arterial Spin Labeling in the Perioperative Management of Carotid Artery Stenting

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Objective: For perioperative management after carotid artery stenting (CAS), it is important to predict hyperperfusion syndrome (HPS). In this study, we qualitatively evaluated cerebral blood flow during the perioperative period following CAS using the pulsed arterial spin labeling (ASL) method, and examined the usefulness of this method. Furthermore, we devised the labeling position so that there was no influence of stenting, reducing errors before and after CAS.

Methods: Of patients with carotid artery stenosis who underwent CAS in our hospital between June 2015 and December 2016, the subjects were 13 in whom ASL could be performed before and after CAS. ASL was performed within 1 week before CAS, as well as 1 and 7 days after CAS. For blood flow assessment, differences in the cerebral cortex at the basal ganglia level between the left and right and between the preoperative and postoperative states after CAS were qualitatively compared.

Results: After CAS, favorable dilation at the lesion site was achieved in all patients. Before CAS, ASL on the affected side showed a reduction in blood flow in nine patients although qualitative assessment was conducted. The day after procedure, findings presage of HP were obtained on ASL in four patients. Of these, HP syndrome-related internal capsule hemorrhage was noted in one case. ASL 7 days after CAS facilitated the assessment of an improvement in cerebral blood flow in comparison with the preoperative state in nine patients.

Conclusion: In perioperative management following CAS, ASL is a rapid, noninvasive procedure, facilitating repeated imaging in a short period. This procedure was useful for evaluating cerebral blood flow.

Keywords ▶ carotid artery stenting, hyperperfusion, arterial spin labeling

Introduction

Recently, carotid artery stenting (CAS) has been widely performed, as it is minimally invasive. However, there are high-risk patients who may develop CAS-related complications.[1)] If hyperperfusion (HP) occurs after CAS, causing convulsion, headache, subarachnoid hemorrhage, and cerebral hemorrhage (hyperperfusion syndrome [HPS]), the prognosis may be deteriorated.[2–5)] Therefore, in the perioperative phase of CAS, postoperative management must be conducted, considering HPS. After CAS, the incidence of HPS complicated by intracranial hemorrhage is higher than after carotid endarterectomy (CEA), and the onset of HPS is earlier (within 12 hours after procedure).[6)] It may be important to extract high-risk patients for HPS based on preoperative state of cerebral circulation, diagnose HP in the early stage, and prevent HPS. Several studies evaluated the cerebral vascular reserve (CVR) using single photon emission computed tomography (SPECT) before CAS, and reported that the risk of postoperative HP was high in patients with a reduction in the CVR.[3–5)] However, SPECT is not always available in all institutions, including our hospital. In this study, we examined whether arterial spin labeling (ASL),[7)] which facilitates qualitative cerebral perfusion imaging with blood as an intrinsic tracer

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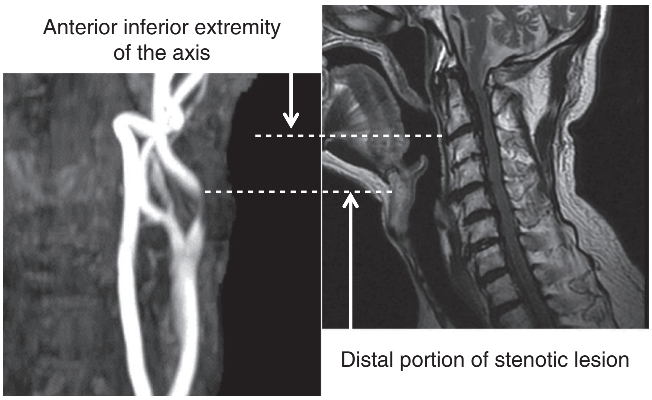
A



B

Pulse sequence	FRFSE – XL
Slice orientation	Sagittal
TR / TE (ms)	1160 (Auto) / 102
FOV (cm)	24
Slice thickness (mm)	5.0 / 1.0
Freq / Phase	256 / 192
Echo train length	24
NEX	3
BW (kHz)	31.25
Scan time (sec)	30

Fig. 1 (**A**) Establishment of the labeling position. Labeling was conducted at an area 6 cm superior to the distal stenotic site, as the labeling position was established as 2 cm inferior to the lower end of a slab. The positional relationship between the lower end of the axis and labeling site was measured, and the patient-inherent imaging position was determined. (**B**) Sequence of localized cervical vertebral images. BW: bandwidth; FOV: field of view; NEX: number of excitations; TE: echo time; TR: repetition time

in the absence of contrast medium through tissue arterial blood labeling, is useful for the diagnosis of HP. Although the reliability of ASL similar to that of conventional examination procedures, such as SPECT and positron emission tomography (PET), has not been established, ASL has the following merits: it is a noninvasive procedure; it requires a low cost; a radionuclide tracer is unnecessary; and it can be conducted several times in a short duration. On the other hand, patients in whom stenting-related artifacts made evaluation impossible were reported. In this study, we established the labeling position so that there was no influence of stenting, devised a measurement method to reduce errors by labeling at the same position before and after stenting, and evaluated cerebral blood flow before and after CAS to examine the usefulness of ASL.

Subjects and Methods

Subjects

Of patients with carotid artery stenosis who underwent CAS in our hospital between June 2015 and December 2016, we retrospectively investigated 13 who underwent arterial ASL-MRI before and after procedure (8 males, 5 females, mean age: 72.7 ± 7.8 years [63–85 years], stenosis of the right internal carotid artery: nine patients).

MRI

We used a SignaHDxt 1.5T MRI system (General Electric Medical Systems, Milwaukee) with an 8chNV ARRAY coil. Imaging conditions were established as follows: sequence, 3D ASL (pCASL); post-labeling delay (PLD), 1525 ms; repetition time (TR)/echo time (TE), 4587/10.5 ms; field of view (FOV), 24 cm; slice thickness, 4.0 mm; bandwidth (BW), 62.5 kHz; scan locs, 32; arm/points, 8/512; and scan time, 4.26 min. ASL images of the entire brain were obtained within 7 days before CAS, as well as 1 and 7 days after CAS. However, when findings suggestive of HP were obtained, ASL imaging was frequently performed to examine serial changes so that the systolic blood pressure was maintained at ≤130 mmHg. For ASL, localized cervical vertebral imaging (fast recovery [FR]-based imaging in 30 seconds) was additionally conducted to avoid unsuccessful imaging related to labeling mistakes, which may occur after stenting, and minimize errors before and after CAS through a constant labeling position. The patient-inherent imaging position was measured from the distance between the lower end of the axis and distal stenotic site (higher position in cases of bilateral internal carotid artery stenosis), and the labeling position was planned so that there was no influence of a stent. It was established as 2 cm inferior to the lower end of a slab so that a pulse reached an area 6 cm superior to the distal carotid artery stenotic site. If soft tissue is used as an index, there may be an error before and after stenting. Therefore, we measured the positional relationship between the lower end of the axis and labeling site, determined the patient-inherent imaging position, and performed labeling so that the same positional relationship from the lower end of the axis was maintained before and after CAS (**Fig. 1**). As it is impossible to quantify cerebral blood flow using perfusion-weighted imaging (PWI) with ASL, the same three neurosurgeons qualitatively evaluated color ASL images at the left and

Table 1 CBF evaluation by ASL after CAS

Case	Age	Gender	CBF compaired between ipsilateral (i) and contralateral (c) hemisphere						Change	HPS
			Pre, ratio		Post (POD1), ratio		Post (POD7), ratio			
1	79	M	+ (i < c)	0.89	+ (i = c)	1.10	+ (i = c)	1.08	+	Not occurred
2	78	M	− (i = c)	1.00	− (i = c)	1.00	− (i = c)	1.01	−	Not occurred
3	75	M	− (i = c)	1.01	− (i = c)	1.01	− (i = c)	1.01	−	Not occurred
4	68	M	+ (i < c)	0.87	+ (i = c)	1.10	+ (i = c)	1.16	+	Not occurred
5	63	F	+ (i < c)	0.93	++ (i > c)	1.25	+ (i = c)	1.18	+	Not occurred
6	65	F	+ (i < c)	0.87	++ (i > c)	1.40	+ (i = c)	1.10	+	Not occurred
7	72	M	− (i = c)	1.00	− (i = c)	1.07	− (i = c)	0.99	−	Not occurred
8	63	F	+ (i < c)	0.90	+ (i = c)	1.18	+ (i = c)	1.02	+	Not occurred
9	65	F	+ (i < c)	0.98	+ (i = c)	1.12	+ (i = c)	1.08	+	Not occurred
10	79	M	+ (i < c)	0.79	++ (i > c)	1.50	+ (i = c)	1.28	+	Hemorrhage
11	85	M	+ (i < c)	0.70	+ (i = c)	1.12	+ (i = c)	1.11	+	Not occurred
12	84	F	− (i = c)	1.01	− (i = c)	1.08	− (i = c)	1.01	−	Not occurred
13	69	M	+ (i < c)	0.94	++ (i > c)	1.20	+ (i = c)	1.16	+	Not occurred

Qualitative ASL-based assessment of CBF changes during the perioperative period after CAS. The preoperative ratio is the affected-/unaffected-side ROI ratio for the cerebral cortex at the basal ganglia level. The ratio immediately after CAS (POD1) is the affected-/unaffected-side ROI ratio for the cerebral cortex at the basal ganglia level. The ratio 7 days after CAS is the cerebral cortex at the basal ganglia level/cerebellum ratio in comparison with the preoperative value. ASL: arterial spin labeling; CAS: carotid artery stenting; CBF: cerebral blood flow; HPS: hyperperfusion syndrome; POD: post operative day; ROI: region of interest

right symmetric sites in the cerebral cortex at the basal ganglia level, as well as those of the affected-side cerebellum and cerebral cortex at the basal ganglia level, before and after CAS. In the 13 subjects, the results of evaluation were consistent among the three neurosurgeons. Patients qualitatively evaluated by all of the three neurosurgeons as showing an increase in cerebral blood flow in comparison with the contralateral side on postoperative color ASL images of the affected-side cerebral cortex at the basal ganglia level were regarded as having HP. We established the region of interest (ROI) using original ASL images of the cerebral cortex at the basal ganglia level and cerebellum, and compared the results through numerization. Due to qualitative ASL images, the values obtained were not quantitative or absolute values, but comparison was possible. Patients with an affected-/unaffected-side ROI ratio of ≤1.0 for the cerebral cortex at the basal ganglia level were regarded as showing a reduction in blood flow before CAS. Furthermore, those with an affected-/unaffected-side ROI ratio of ≥1.2 for the cerebral cortex at the basal ganglia level were regarded as showing an increase in blood flow immediately after procedure. Those with a ≥1.0-fold increase in the cerebral cortex/cerebellum ratio at the basal ganglia level after CAS in comparison with the preoperative value were regarded as showing an increase in blood flow 7 days after CAS in comparison with the preoperative value (**Table 1**). Carotid artery revascularization was indicated for ≥50% symptomatic stenosis or ≥80% asymptomatic stenosis on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (cerebral angiography). CAS was indicated for high-risk patients for CEA. CEA or CAS was individually selected based on lesion access, plaque volume/properties, and mural thrombus formation. During the same period, CEA was performed for five patients. All symptomatic lesions were treated in the chronic phase, ≥3 weeks after onset. Concerning surgical procedures, the oral administration of aspirin at 100 mg/day and clopidogrel at 75 mg/day was started ≥1 week before CAS, and, in patients receiving anticoagulant or cilostazol therapies, each therapy was also combined during the perioperative period. CAS was performed under systemic heparin administration (target activated clotting time: 300 seconds) using a transfemoral approach under local anesthesia. A guiding catheter with a balloon was inserted into the common carotid artery, and embolic protection devices (distal filter: one patient, distal balloon: 12 patients) were used in all patients. As all patients had symptomatic lesions or stenotic lesions with unstable plaque properties, a closed-cell stent (Carotid Wallstent; Boston Scientific, Natick, MA, USA) was used. A stent diameter 1–2 mm larger than the diameter of the common carotid artery was adopted. For postdilation, we used a balloon of which the diameter was approximately 80% of the normal diameter of the distal internal carotid artery. After CAS, neither heparin reversal nor continuous administration was conducted. The blood pressure was strictly controlled so that the systolic blood pressure was ≤130 mmHg until 72 hours after CAS.

Results

Concerning CAS procedures, stenting involving the internal to common carotid arteries was performed for all patients, and favorable dilation of stenotic lesions was achieved (≥75% of the normal diameter of the distal internal carotid artery). During postoperative follow-up, there was no patient with persistent bradycardia (pulse: <50/min) or hypotension requiring the continuation of vasopressor administration, with a systolic blood pressure of <90 mmHg. A summary of the 13 subjects is shown in **Table 1**. HPS-related internal capsule hemorrhage occurred in one patient. There was no perioperative major/minor ischemic stroke in any patient. Before CAS, ASL on the affected side showed a reduction in cerebral blood flow in nine patients (0.88 ± 0.08, range: 0.71–0.98). In four of these, ASL the day after CAS showed an increase in cerebral blood flow on the affected side (1.34 ± 0.14, range: 1.25–1.50) in comparison with contralateral cerebral blood flow, suggesting HP. Even in the patient with internal capsule hemorrhage, findings suggestive of HP were obtained from 12 until 36 hours after procedure, and sedative/hypotensive therapies were conducted. In four patients without a reduction in cerebral blood flow in comparison with contralateral blood flow on ASL on the affected side before CAS, blood flow on the affected side the day after CAS was similar to preoperative or contralateral blood flow (1.04 ± 0.04, range: 1.00–1.08); there were no findings suggestive of HP. In the nine patients with a reduction in cerebral blood flow on ASL on the affected side before CAS, there was a marked increase in cerebral blood flow in comparison with preoperative blood flow 7 days after CAS (1.13 ± 0.07, range: 1.02–1.28).

Representative cases

A patient in whom postoperative ASL-based assessment was impossible due to stenting-related failure in labeling.

The patient was an 80-year-old male. Watershed infarcts occurred in the right cerebral hemisphere. On MRA, the signal intensity of the right internal carotid artery was reduced. Cerebral angiography revealed 99% stenosis at the origin of the right internal carotid artery (NASCET method) and the stenosis was as high as the C2-4 vertebrae. The internal carotid artery showed pseudo-occlusion, and the blood flow of the internal carotid artery was delayed in comparison with that of the external carotid artery. Carotid ultrasonography showed a low-echoic plaque. On T1-weighted MR images of the carotid artery, the signal intensity of plaque was high, suggesting unstable plaque. Preoperative ASL suggested a reduction in cerebral blood flow on the affected side. A guiding catheter with a balloon was guided into the right common carotid artery. On passing a distal protection device, proximal blockage was conducted, and pre-dilation was performed under distal balloon protection. Subsequently, a Carotid Wallstent 8 × 29 mm was inserted, and postdilation was conducted. As the stenotic site was present at a relatively high position, the labeling position overlapped with the site of stenting when adopting the autolabeling method; postoperative ASL-based assessment was impossible (**Fig. 2**).

A patient with an improvement in cerebral blood flow on the affected side to the level of contralateral cerebral blood flow after stenting (Case 9).

The patient was a 65-year-old female. Left internal CAS was performed 3 months earlier, and right CAS was planned because subcortical infarction of the right frontal lobe occurred. On cephalic MRA, the signal intensity of the right internal carotid artery was reduced. Cerebral angiography showed 85% stenosis with ulceration at the origin of the right internal carotid artery (NASCET method) and the stenosis was as high as the C2-3 vertebra. Stenosis of the right internal carotid artery was rapidly progressed, and the blood flow of the internal carotid artery was delayed in comparison with that of the external carotid artery. Carotid ultrasonography showed that the culprit plaque was heterogeneously low- to iso-echoic. On T1-weighted MR images of the carotid artery, the signal intensity of plaque was high, suggesting unstable plaque. Preoperative ASL suggested a reduction in perfusion on the affected side. A guiding catheter with a balloon was guided into the right common carotid artery, and a distal protection balloon was passed through proximal blockage. Under distal balloon protection, predilation was conducted. A Carotid Wallstent 8 × 29 mm was inserted, and postdilation was performed. Postoperative ASL showed an improvement in blood flow on the affected side to the level of contralateral blood flow (**Fig. 3**).

A patient in whom an increase in cerebral blood flow on the affected side in comparison with contralateral blood flow (HP) after stenting led to cerebral hemorrhage (HPS) (Case 10).

The patient was an 80-year-old male. He developed multiple infarcts with exacerbation in the watershed area of the right cerebral hemisphere. Preoperative systemic investigation indicated an abdominal aortic aneurysm and progressive advanced gastric cancer. For detailed examination of infarction, cephalic MRA was performed. The visualization signal intensity of the right internal carotid artery was reduced unfavorable. Cerebral angiography showed 90% stenosis at the origin of the right internal carotid artery (NASCET method) and the stenosis was as high as the C1-3 vertebrae. Moreover, the plaque volume was large.

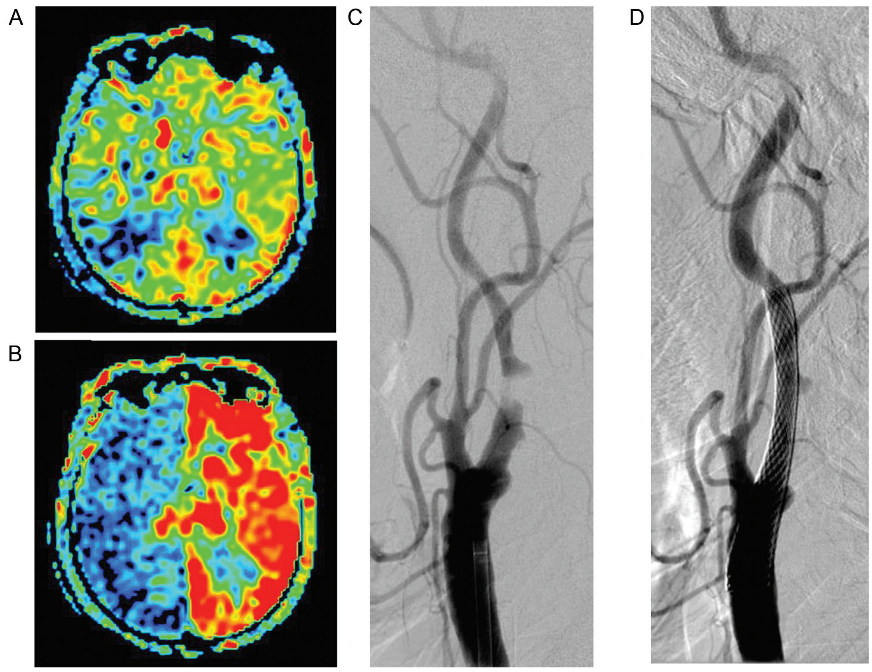


Fig. 2 An 80-year-old male in whom stenting-related failure in labeling affected postoperative ASL-based assessment. (**A**) Preoperative ASL. (**B**) ASL was performed using the autolabeling method the day after CAS. The labeling position overlapped with the site of stenting, making evaluation impossible. (**C**) Marked stenosis at the origin of the right internal carotid artery on preoperative cerebral angiography. (**D**) Reduction of right internal carotid artery stenosis on postoperative cerebral angiography. ASL: arterial spin labeling; CAS: carotid artery stenting

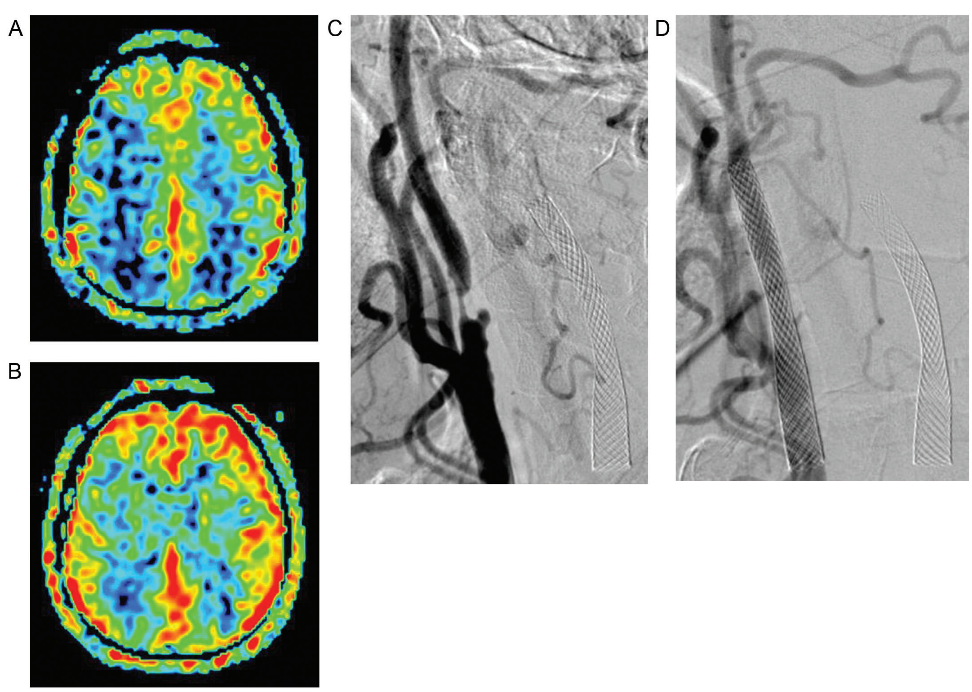


Fig. 3 A 65-year-old female in whom ASL assessment during the perioperative period after CAS was effective. (**A**) Preoperative ASL. (**B**) ASL the day after CAS. (**C**) Preoperative cerebral angiography showed marked stenosis at the origin of the right internal carotid artery. (**D**) Postoperative cerebral angiography confirmed the reduction of internal carotid artery stenosis. ASL: arterial spin labeling; CAS: carotid artery stenting

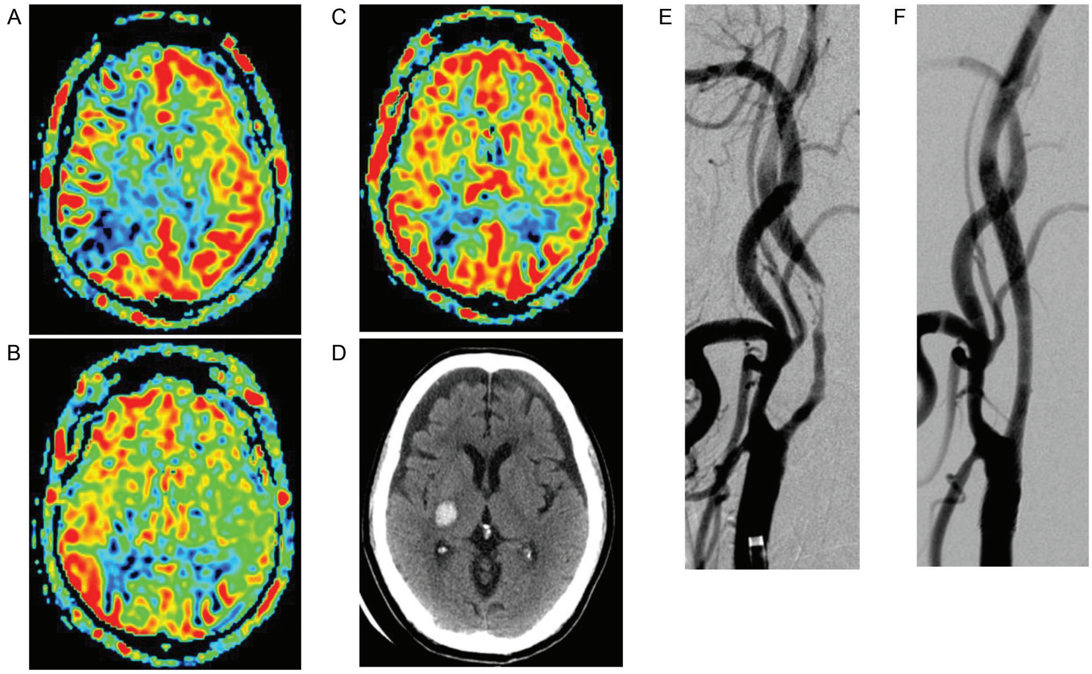


Fig. 4 An 80-year-old male in whom ASL during the perioperative period after CAS facilitated HPS assessment. (**A**) Preoperative ASL. (**B**) ASL the day after surgery CAS. (**C**) ASL 7 days after CAS. (**D**) Cephalic CT the day after CAS revealed right internal capsule hemorrhage. (**E**) Preoperative cerebral angiography showed marked stenosis of the right internal carotid artery. (**F**) Postoperative cerebral angiography confirmed the reduction of internal carotid artery stenosis. ASL: arterial spin labeling; CAS: carotid artery stenting; HPS: hyperperfusion syndrome

Carotid ultrasonography showed a low-echoic plaque. On T1-weighted MR images of the carotid artery, the signal intensity of plaque was high, suggesting unstable plaque. Preoperative ASL suggested a reduction in perfusion on the affected side. Considering the cancer-bearing state and risk of general-anesthesia-related hypotension, CAS was selected. The collateral pathway was not abundant, and the patient was regarded as belonging to a high-risk group for HPS; CAS was conducted. Pre-dilation was performed under distal balloon protection using a transbrachial approach, and a Carotid Wallstent 8 × 29 mm was inserted. During procedure, there was no new neurological deficit. After CAS, blood pressure control was strictly conducted, targeting a systolic blood pressure of <120 mmHg. However, ASL the day after CAS showed an increase in blood flow in the middle cerebral artery (MCA) region on the affected side in comparison with contralateral blood flow, suggesting HP. Subsequently, blood pressure control was strictly performed, but HPS-related cerebral hemorrhage on the affected side occurred 16 hours after CAS. ASL was conducted every day, and strict blood pressure control was continued until the blood flow volume in the MCA region on the affected side became similar to that on the contralateral side. The preoperative modified Rankin Scale (mRS) score was 4, but the patient was discharged after 3-month rehabilitation, with an mRS score of 3 (**Fig. 4**).

Discussion

In institutions without imaging devices that facilitate the quantitative evaluation of cerebral blood flow, such as PET and SPECT systems, including our hospital, it was difficult to evaluate cerebral blood flow and predict the onset of HPS in patients with a reduction in activities of daily living (ADL) due to cerebral-infarction-related sequelae or those who were unable to undergo SPECT in another institution during the perioperative period, involving the day after CAS. ASL provides information on the state of cerebral perfusion although it facilitates qualitative evaluation. Several studies indicated its usefulness for the prediction of HPS and postoperative assessment of cerebral blood flow.[8–10] In the ASL method, proton in arterial blood is labeled with inversion pulse, facilitating brain tissue blood flow imaging through labeled arterial blood transfer into capillary blood vessels and exchange for cerebral parenchymal proton; when the volume of labeled arterial blood is larger, the blood flow volume may be greater. Therefore, for ASL, contrast medium is not necessary, and this is a noninvasive, safe method that facilitates cerebral blood flow measurement in a few minutes; there is no radiation exposure, differing from nuclear medical procedures, such as PET with 150-labeled water and SPECT with radionuclide tracers. In addition, there is no need to wait until a radioactive substance is excreted; therefore, measurement can be repeatedly conducted in a short period. A study compared ASL with SPECT reported that the resting cerebral blood flow and CVR values were consistent between the two procedures. Another study suggested that a large blood flow volume on SPECT is evaluated as much greater on ASL, but assessment based on individual images indicated that ASL provided SPECT-like images.[11,12] However, ASL signals are influenced by various factors, such as the blood flow volume, heart function-related changes in blood flow, cerebral vascular beds, residual spins in the intracranial vessels, and artifacts, due to the principles of ASL.[13] Therefore, we must always consider that cerebral blood flow may be misevaluated.

As a pitfall of ASL, ASL signals may be influenced by metal artifacts.[14] Stent-related artifacts in the cervical region may make labeling impossible, as reported for non-evaluable patients; ASL images cannot be obtained. In this study, errors related to differences in the labeling position in the process of labeling to image acquisition were reduced by avoiding stent-related artifacts after CAS and establishing a constant labeling position before and after CAS. We could avoid the labeling position overlapping the stent after CAS by conducting labeling at an area superior to the stenting position predicted based on localized cervical vertebral images before CAS. In this study, when establishing the labeling position, there was no stent-related artifact in any patient. As the labeling position before CAS was similar to that after CAS, the influence of errors in the labeling position on the time for labeled blood to be distributed in the brain may have been minimized.

As the limitations of ASL images, favorable blood flow images are not obtained when the circulation time is prolonged because labeled arterial blood is influenced by the circulation time. In addition, differences in the circulation time in the slice may modify blood flow information. A study reported that approximately 1.5 seconds were required until labeled blood was distributed in the brain of healthy adults. Considering this interval, the period from labeling until data collection is established. However, ASL images depend on the PLD.[15] In this study, we performed ASL imaging at 3 points, 1.5, 2.0, and 2.5 seconds, examined the results, and established the PLD as 1.5 seconds, at which there was the most marked difference between the unaffected and affected sides. In particular, a study indicated that short-PLD (1000/1500 msec) ASL images were correlated with CBF/CBV on SPECT or ^{15}O-PET; the PLD established in this study may have been appropriate.[16] Another study suggested that an area perfused via delayed blood inflow into the tissue can be evaluated as the state of a collateral pathway by establishing several PLDs.[17] In the future, it may be necessary to establish several PLDs and review several images in a larger number of patients.

Of the 13 subjects, 9 showed a reduction in blood flow on ASL on the affected side before CAS. In four of these, HP could be diagnosed from a result of ASL images the day after CAS. In the four patients, strict blood pressure control was conducted. HPS, in which HP causes headache, restlessness, convulsion, or intracranial hemorrhage, may deteriorate the prognosis of patients. In particular, intracranial hemorrhage is a serious complication,[6] as demonstrated in Case 10. In patients with HP, strict blood pressure control is necessary, and even a type of asymptomatic HP, hyperperfusion phenomenon (HPP), may induce the deciduation of neurons involving the entire cerebral cortex, leading to higher brain dysfunction;[18] therefore, it is important to predict the development of HP and perform strategies to prevent HP. In this study, we evaluated ASL images alone without comparing them with SPECT findings, but it was possible to predict HPS. When ASL findings suggested HP, early HP diagnoses and subsequent adequate management with hypotensive drugs may have contributed to the prevention of deterioration to HPS. In particular, ASL images can be repeatedly obtained in a short period, differing from SPECT. We could evaluate serial changes in cerebral blood flow. Furthermore, HP was absent in all four patients without findings suggestive of a reduction in blood flow on the affected side before CAS.

In this study, we examined the usefulness of ASL during the perioperative period after CAS. The reliability of ASL similar to that of conventional examinations, such as SPECT and PET, has not been established, but ASL can be simultaneously performed in combination with MRA or diffusion-weighted imaging (DWI). ASL was useful for evaluating the condition, as it provided information on perfusion in addition to ischemic changes or vascular information. For HPS prevention, it is important to promote strategies in advance. Although ASL does not have any quantitative property, a study reported that the resting cerebral blood flow value was consistent with that on SPECT;[11]

therefore, even ASL alone facilitates evaluation, and it may be useful for preventing HPS in clinical practice. In the future, PLD conditions or image assessment methods must be reviewed in a larger number of patients.

Conclusion

For perioperative management after CAS, cerebral blood flow assessment with ASL, which is a rapid, noninvasive procedure that facilitates repeated imaging, was useful. Furthermore, stenting-related artifacts and labeling-position-related errors could be reduced by establishing a constant labeling position, and this contributed to HP diagnosis in the perioperative management of carotid artery stenosis. However, ASL signals are influenced by various factors in addition to the blood flow volume due to the principles of ASL; therefore, caution is needed for image assessment to evaluate the condition. This study indicated that ASL was useful as a screening method for cerebral circulation assessment to predict HP during the perioperative period after CAS. However, the reliability of ASL similar to that of ^{15}O-PET or SPECT has not been established. In the future, further development, including quantification, may be necessary.

Disclosure Statement

There is no conflict of interest for the first author and coauthors.

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