Online August 18, 2020
Journal of Neuroendovascular Therapy 2020; 14: 475–480 DOI: 10.5797/jnet.oa.2019-0109

Original Article

Effects of Aspiration and Re-transfusion Technique with Carotid Artery Stenting

Yoshiaki Tokuyama, Tatsuro Takada, Noriko Usuki, Satoshi Takaishi, Kentaro Tatsuno, Yuki Hamada, Haruki Otubo, and Toshihiro Ueda

Objective: Embolic stroke is the most serious complication after carotid artery stenting (CAS). The incidence rate of embolic stroke is reduced by the use of embolic protection devices (EPDs); however, there is no consensus on which EPD is the most effective. The aspiration and re-transfusion technique (ART) with CAS under distal balloon protection was adopted at our center to reduce the incidence of embolic complications. This retrospective study investigated the effects of ART.
Methods: From November 2010, 243 consecutive patients treated by CAS under distal balloon protection were included. ART was performed on 202 patients (ART group) and the other 40 patients only received distal balloon protection (non-ART group). In ART, the blood from the aspiration catheter was continuously returned through a filter to the femoral vein. The amount of debris was assessed intermittently using a small blood sample and the rest was returned. We investigated the diffusion-weighted imaging (DWI)-positive rate and symptomatic ischemic stroke one day after CAS.
Results: Compared with the non-ART group, the incidence of DWI-positive lesions (22.7% vs 37.5%, P = 0.07) and frequency of symptomatic ischemic stroke (0.9% vs 5.0%, P = 0.12) were reduced in the ART group. The hemoglobin reduction rate was significantly reduced by ART (11.1% vs 14.9%, P <0.01). In the ART group, the frequency of multiple lesions (more than 5) and large lesions (more than 10 mm) was lower than that in the non-ART group (P <0.01, P = 0.14).
Conclusion: CAS under distal balloon protection with ART was effective at reducing the incidence of DWI-positive lesions and may be useful to reduce the incidence of symptomatic ischemic stroke.

Keywords ▶ carotid artery stenting, distal balloon protection, distal embolic protection device

Introduction

Carotid artery stenting (CAS) has been demonstrated to be useful to treat carotid artery stenosis in several randomized controlled studies,[1–3] but the incidence of embolic stroke, one of the most important complications, was reported to be higher than that after carotid endarterectomy (CEA).[4] The risk of embolic stroke is considered to be high in carotid artery stenosis patients with vulnerable plaques.[5]

On the other hand, the use of an embolic protection device (EPD) is essential to prevent embolic stroke in CAS regardless of the presence of vulnerable plaques. However, no randomized controlled study has reported which EPD most markedly reduces the incidence of stroke, and its selection is at the discretion of each facility and operator.

At our hospital, active aspiration is performed until sufficient reduction of debris in aspirated blood is acquired to prevent distal embolus. However, there have been difficulties such as postoperative anemia due to a large volume of blood aspiration and completion of the aspiration procedure before confirming sufficient debris reduction. To address these problems, we designed the aspiration and re-transfusion technique (ART) under distal balloon protection and initiated CAS using ART in December 2011. The objective of this study was to investigate the treatment outcomes of CAS using ART during the 7-year period.

Department of Strokology, Stroke Center, St. Marianna University Toyoko Hospital, Kawasaki, Kanagawa, Japan

Received: December 9, 2019; Accepted: June 9, 2020
Corresponding author: Yoshiaki Tokuyama. Department of Strokology, Stroke Center, St. Marianna University Toyoko Hospital, 3-435, Kosugimachi, Nakahara-ku, Kawasaki, Kanagawa 211-0063, Japan
Email: hsmtoku555@marianna-u.ac.jp

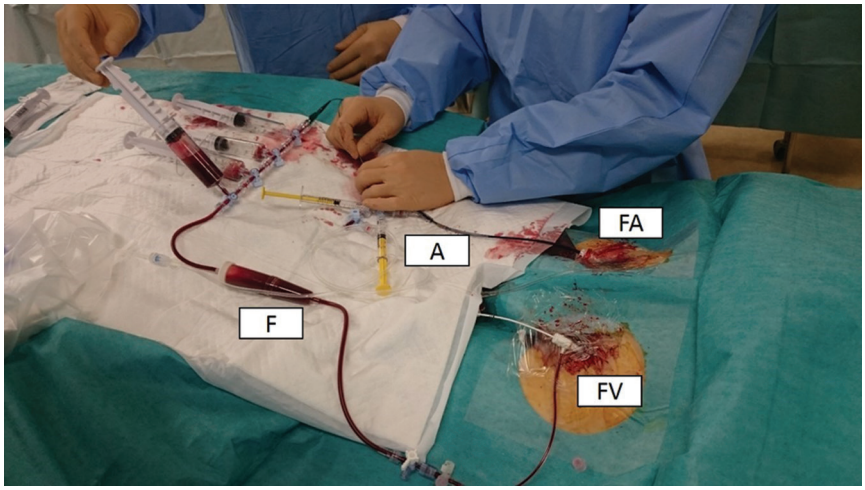

Fig. 1 The ART with CAS under distal balloon protection. Blood is aspirated by moving an aspiration catheter upward and downward in the region from the lesion to the distal balloon protection region. The aspiration catheter is connected to a direct three-way stopcock to prepare a closed circuit and blood is sequentially aspirated through a four-way connection of syringes. Aspiration can be continued even during re-transfusion from the near-side syringe. Aspirated blood is returned to the contralateral femoral vein through a filter. Aspirated blood is discarded from the body through a filter using the foremost (arterial side) syringe every 4 or 8 syringes, and the presence of debris is confirmed. A: aspiration catheter; ART: aspiration and re-transfusion technique; CAS: carotid artery stenting; F: filter; FA: femoral artery sheath; FV: femoral vein sheath

Materials and Methods

The subjects were 242 patients treated by CAS under distal balloon protection using Carotid Guardwire PS (Medtronic, Dublin, Ireland) at our hospital between November 2010 and July 2018 (mean age: 79.3 ± 7.7 years old, male: 88.0%). The non-ART group was composed of 40 consecutive patients between November 2010 and November 2011, the ART group was composed of 202 consecutive patients from December 2011, and the treatment outcomes of each group were retrospectively investigated and compared.

The indication criteria were 50% or higher symptomatic or 70% or higher asymptomatic arteriosclerotic stenosis in the carotid artery on carotid artery echo or angiography. Acute-phase stroke (within 7 days), arterial dissection, and re-stenosis lesions after CAS were excluded. In addition, patients on whom MRI was unable to be performed on the day following treatment due to reasons, such as pace maker placement, were excluded. In the CAS technique, sedation by continuous intravenous administration of propofol was applied under local anesthesia as needed in all patients. An 8-Fr sheath was placed by femoral arterial puncture and a 3-Fr sheath was placed in the contralateral femoral vein in the ART group. For the guiding catheter, an 8-Fr OPTIMO (Tokai Medical products, Inc., Aichi, Japan) was placed in the ipsilateral common carotid artery. In all patients, treatment was performed under distal blood flow blockage by a balloon placed in the distal ICA, which was passed through the lesion using a Guardwire under proximal blood flow blockage by OPTIMO and then placed in the distal ICA. Predilation was applied in all patients. For the carotid artery stent, PRECISE (Cordis, Fremont, CA, USA), Carotid Wallstent (Boston Scientific, Natick, MA, USA), and PROTAGE (Medtronic, Irvine, CA, USA) were used. After the addition of post-dilation as needed, blood was aspirated using an aspiration catheter. In the non-ART group, aspiration was continued using a 20-mL syringe until debris disappeared or was reduced to a visual minimum, and all aspirated blood was discarded from the body. In the ART group, aspirated blood was returned to the venous side in a closed circuit.

The employed ART method is shown in **Fig. 1**. After stent placement under distal balloon protection or post-dilation, blood was aspirated using an aspiration catheter and aspirated blood was returned from the sheath placed in the contralateral femoral vein through a filter in the closed circuit. Debris in aspirated blood was intermittently assessed and distal balloon protection was removed after confirming sufficient reduction of debris. All aspirated blood, excluding that in the syringe used to check debris, was returned to the femoral vein. The presence of occlusion of intracranial blood vessels was confirmed on final imaging to complete the technique.

Table 1 Baseline characteristics

	ART	Non-ART	P
N	202	40	–
Age, ave. ± SD	73.9 ± 8.06	73.7 ± 7.97	0.86
Female, n (%)	25 (12.3)	4 (10.0)	0.79
HT, n (%)	171 (84.6)	33 (82.5)	0.81
DM, n (%)	84 (41.5)	16 (40.0)	1
HLP, n (%)	132 (65.3)	24 (60.0)	0.58
Smoking, n (%)	114 (56.4)	26 (65.0)	0.38
Af, n (%)	10 (4.95)	3 (7.50)	0.45
Ipsilateral ischemic event, n (%)	102 (50.4)	26 (65.0)	0.09

Af: atrial fibrillation; ART: aspiration and re-transfusion technique; DM: diabetes mellitus; HLP: hyperlipidemia; HT: hypertension

Table 2 Ipsilateral DWI-positive rate, frequency of symptomatic cerebral infarction, and the effect of ART on postoperative anemia

	ART	Non-ART	P
N	202	40	–
Ipsilateral DWI-positive lesion, n (%)	46 (22.7)	15 (37.5)	0.07
Symptomatic ischemic stroke, n (%)	2 (0.9)	2 (5.0)	0.12
Total aspiration blood volume, mL (Ave. ± SD)	396.8 ± 173.1	265.5 ± 112.2	<0.001
Disposal blood volume, mL (Ave. ± SD)	94.6 ± 40.4	265.5 ± 112.2	<0.001
Hb (pre operation), g/dL (Ave. ± SD)	12.6 ± 1.62	12.5 ± 1.58	0.61
Hb (postoperation day1), g/dL (Ave. ± SD)	11.2 ± 1.50	10.7 ± 1.84	0.04
Hb lowering rate, % (Ave. ± SD)	11.1 ± 6.11	14.9 ± 7.09	0.01

ART: aspiration and re-transfusion technique; DWI: diffusion-weighted imaging; Hb: hemoglobin

Diffusion-weighted imaging (DWI) MRI was performed on all patients on the day following CAS. In patients in whom high-intensity areas were noted on the ipsilateral side of treatment, the number and rate of high-intensity areas were evaluated as the ipsilateral DWI-positive rate. In addition, the incidence of symptomatic stroke was investigated during CAS and the 24-hour postoperative period. Furthermore, blood was collected before treatment and after the day following treatment, and anemia was evaluated based on changes in the hemoglobin level. In addition, the duration of blood flow blockage by distal balloon protection and the presence of intolerance symptoms induced by blood flow blockage-induced ischemia were investigated.

For between-group comparison, Fisher's exact test or chi-square test was used. For statistical analysis, JMP pro (SAS Institute, Cary, NC, USA) was used and $P < 0.05$ was regarded as significant.

Results

The patient background is shown in **Table 1**. No significant difference was noted in the age or sex ratio between the ART and non-ART groups. In all 242 patients, hypertension was the most common risk factor for arteriosclerosis, accounting for 84.3% of all patients. No significant difference was noted in each risk factor between the two groups. Symptomatic lesions were noted in 102 patients (50.4%) in the ART group and 26 (65.0%), being higher in the non-ART group ($P = 0.09$).

In the ART group, the ipsilateral DWI-positive rate on the day following treatment was 22.7% and the incidence of symptomatic stroke was 0.9%, being lower than those (37.5 and 5.0%, respectively) in the non-ART group, but the differences were not significant ($P = 0.07$, 0.12). Symptomatic stroke did not develop in 112 consecutive patients after January 2015 in the ART group.

The mean total volume of aspirated blood during the procedure in the non-ART group was 265.5 mL and this volume was discarded from the body. In the ART group, 396.8 mL was aspirated on average. Excluding blood for re-transfusion, the blood volume discarded from the body was 94.6 ± 40.4 mL. The Hb reduction rate based on comparison between the preoperative blood Hb level and blood Hb level on the day following treatment was 11.1% in the ART group and 14.9% in the non-ART group, being significantly lower in the ART group ($P = 0.01$) (**Table 2**).

Table 3 Characteristics of ipsilateral DWI-positive lesions

	ART	Non-ART	P
Ipsilateral DWI-positive lesion, n (%)	46 (22.7)	15 (37.5)	0.07
Number of lesions			
1, n (%)	24 (52.1)	6 (40.0)	
2–4, n (%)	20 (43.4)	4 (26.6)	
5≤, n (%)	2 (4.3)	5 (33.3)	
Median (Q1–Q3)	1 (1-2)	3 (1-5)	<0.01
Large (≥10 mm) lesion, n (%)	7 (15.2)	5 (33.3)	0.14

ART: aspiration and re-transfusion technique; DWI: diffusion-weighted imaging

The characteristics of ipsilateral DWI high-intensity lesions in the ART and non-ART groups are shown in **Table 3**. Of the 46 ipsilateral DWI-positive patients, only one lesion was present in 24 patients (52.1%) and the median number of lesions was 1 and 3 in the ART and non-ART groups, respectively, being significantly lower in the ART group ($P < 0.01$). In addition, 10-mm or larger lesions were present in many patients in the non-ART group, but there was no significant difference (15.2% vs. 33.3%, $P = 0.14$) (**Table 3**).

In the ART group, the median duration of blood flow blockage in all CAS cases was 21 minutes, and the median time required for aspiration and re-transfusion alone was 11 minutes. Transient neurological manifestation due to intolerance developed in none of the patients in the non-ART group and five (2.5%) patients in the ART group. No intolerance-induced stroke or permanent sequela remained in any patient.

Discussion

Previous large-scale studies reported that the treatment effects of CAS for carotid artery stenosis were comparable to those of CEA in patients with normal CAE risk, but the incidence of postoperative embolic stroke is generally higher in CAS cases.[1,2,6–8] In a recent meta-analysis, it was concluded that CAS may increase the risk for perioperative stroke compared with CEA.[4]

Therefore, the role of EPDs is important to prevent stroke after CAS. However, no randomized controlled study has reported which EPD most markedly reduced the incidence of stroke. In the MAVErIC study using a distal balloon-type device, ipsilateral embolic stroke was noted in 3.0%.[9] In contrast, in CREST and ACT-1 studies using a filter type, the incidences of ipsilateral embolic stroke were 3.8 and 2.4%, respectively.[2,3] Furthermore, in the ARMOUR study using a proximal balloon occlusion-type device, MO.MA (Invatec, Roncadelle, Italy), the incidence of ipsilateral embolic stroke was 2.3%.[10] These studies suggested that it is difficult to judge the superiority of a single EPD at present.

For CAS under distal balloon protection, no criterion for the frequency or total amount of debris aspiration has been specified.[6,11] In actual clinical practice, the frequency is decided beforehand or the timing of aspiration completion is decided while confirming the amount of actual debris based on the judgment at each facility. At our hospital, considering that reliable confirmation of sufficient reduction of aspirated blood debris is important to prevent distal embolus, active blood aspiration has been performed before ART. However, we encountered patients in whom debris was not sufficiently reduced or gradually increased even though aspiration was repeated many times. Moreover, the aspiration procedure was inevitably completed before confirming sufficient debris reduction, risking the development of postoperative anemia requiring blood transfusion. The introduction of ART increased the mean total volume of blood aspiration from 266.3 to 384.5 mL with re-transfusion of approximately 300 mL, and the mean blood volume actually discarded was able to be reduced to 94 mL on average. This corresponds to approximately five 20-mL syringes, being a valid volume comparable to that in CAS employing the general distal occlusion method. In addition, the preoperative Hb level was slightly reduced from 12.5 to 10.7 g/dL after treatment in the non-ART group, whereas the decrease was slight, from 12.6 to 11.2 g/dL, in the ART group. However, a volume of 300 mL or larger is not generally aspirated in CAS, and it is necessary to investigate the application of this massive aspiration to all patients. Indeed, the total blood aspiration volume widely ranged from 60 to 240 mL in our study and the total blood aspiration volume may change depending on the conditions, such as the presence and amount of vulnerable plaques; therefore, it is necessary to continue investigating the true indications of ART. Satoh et al.[12] reported the usefulness of autotransfusion of aspirated blood after CAS using a blood bag, in which blood aspiration

was continued until debris became unable to be confirmed, resulting in a large variation in the autotransfusion volume from 100 to 2000 mL (mean: 309.5 mL) among patients.

In our study, the DWI-positive rate was 22.7% in the ART group, being lower than that in the non-ART group. The rate of DWI high-intensity lesions on angiography or after CAS varied from 12.9 to 87.1% among reports.[13,14] On the other hand, in a recent systematic review, the rate was 18.1% in CEA cases and 40.5% in CAS cases, being relatively high,[5] and the DWI-positive rate limited to ipsilateral CAS cases was 38.1%. In our study, the DWI-positive rate was relatively low and the incidence of symptomatic stroke was 0.9%, being very low. Furthermore, two patients who developed symptomatic stroke had non-disabling stroke. The incidence in our study was lower than that of 3.8% in the CREST study,[1] 2.4% in the ACT1 study,[2] and 3.0% in the MAVErIC study using the same distal balloon- type device. In addition, symptomatic stroke did not develop in any of the 112 patients after 2015, suggesting the involvement of the proficiency in the ART technique.

Of note, DWI high-intensity lesions were single punctiform high-intensity lesions in many patients in the ART group. Gensicke et al. previously reported that the volume of postoperative DWI-positive lesions after CAS was smaller than that after CEA, but the number of lesions was large, being characteristic.[15] Ohashi et al. discussed the symptomatic stroke-preventive effects of tailored CAS which uses an appropriate EPD based on the diagnosis of plaques before CAS. They hypothesized that the number of DWI-positive lesions decreased from before the introduction of tailored CAS and that this played a role in the effects.[16] Accordingly, suppression of an increase in the postoperative volume of DWI-positive lesions after CAS by inhibition of the number lesions may be an important element to prevent symptomatic stroke. The use of ART safely increased the total aspirated blood volume without aggravating anemia, reducing the risk of multiple and large embolism, which may have helped reduce the incidence of symptomatic stroke.

The biggest problem of ART is the prolongation of blood flow blockage with an increase in the frequency of aspiration. Attention should be paid to the use of ART in patients with a low baseline ischemic tolerance, especially in those with contralateral carotid artery occlusion. Contralateral carotid artery occlusion did not develop in any patient, but intolerance-induced transient neurological manifestation after treatment was observed in 2.5% of patients. Evaluation of preoperative ischemic tolerance, an increase in the efficiency of re-transfusion of aspiration, and shortening of the time are tasks to be addressed in the future.

This study had several limitations. It was a single-center retrospective study, reduction of debris was confirmed during ART, the duration of aspiration was at the operator's discretion, being variable, and the CAS technique has a risk of causing distal embolus during guide catheter placement and passing through the lesions, in addition to the risk of debris scattering during stent placement, limiting evaluation of the effects of ART such as those on the DWI-positive rate on the day following treatment and symptomatic stroke.

Conclusion

CAS using ART under distal balloon protection may reduce the postoperative ipsilateral DWI-positive rate and incidence of symptomatic stroke.

Disclosure Statement

The authors declare no conflicts of interest.

References

1) Jay S. Yadav, Mark H, et al: Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004; 351: 1493–1501.
2) Brott TG, Hobson RW II, Howard G, et al: Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010; 363: 11–23.
3) Rosenfield K, Matsumura JS, Chaturvedi S, et al: Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med* 2016; 374: 1011–1020.
4) Moresoli P, Habib B, Reynier P, et al: Carotid stenting versus endarterectomy for asymptomatic carotid artery stenosis: a systematic review and meta-analysis. *Stroke* 2017; 48: 2150–2157.
5) Rots ML, Meershoek AJA, Bonati LH, et al: Editor's choice - predictors of new ischaemic brain lesions on diffusion weighted imaging after carotid stenting and endarterectomy: a systematic review. *Eur J Vasc Endovasc Surg* 2019; 58: 163–174.
6) Jean-Louis Mas, Gilles Chatellier, Bernard Beyssen, et al: Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *N Engl J Med* 2006; 355: 1660–1671.
7) SPACE Collaborative Group, Ringleb PA, Allenberg J, et al: 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic

patients: a randomised non-inferiority trial. *Lancet* 2006; 368: 1239–1247.

8) International Carotid Stenting Study investigators: Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. *Lancet* 2010; 375: 985–997.
9) Hamner JW, Tan CO, Lee K, et al: Sympathetic control of the cerebral vasculature in humans. *Stroke* 2010; 41: 102–109.
10) Ansel GM, Hopkins LN, Jaff MR, et al: Safety and effectiveness of the INVATEC MO.MA proximal cerebral protection device during carotid artery stenting: results from the ARMOUR pivotal trial. *Catheter Cardiovasc Interv* 2010; 76: 1–8.
11) Henry M, Henry I, Polydorou A, et al: Carotid angioplasty and stenting under cerebral protection with the Percusurge Guardwire system. *J Interv Cardiol* 2004; 17: 233–243.
12) Satoh K, Hanaoka M, Tamura T, et al: Transition of carotid artery stenting (Cas) treatment in the multiple device era (effectiveness of distal balloon protection CAS treatment using an autologous aspirated blood transfusion). *Surg Cereb Stroke (JPN)* 2015; 43: 347–351. (in Japanese)
13) Bijuklic K, Wandler A, Hazizi F, et al: The PROFI study (prevention of cerebral embolization by proximal balloon occlusion compared to filter protection during carotid artery stenting): a prospective randomized trial. *J Am Coll Cardiol* 2012; 59: 1383–1389.
14) Sawada M, Yasokawa Y, Mizutani D: Appropriate selection of CAS or CEA and proper use of protection device in the event of CAS according to carotid plaque characteristics. *J Neuroendovasc Ther* 2016; 10: 190–195.
15) Gensicke H, Zumbrunn T, Jongen LM, et al: Characteristics of ischemic brain lesions after stenting or endarterectomy for symptomatic carotid artery stenosis: results from the international carotid stenting study-magnetic resonance imaging substudy. *Stroke* 2013; 44: 80–86.
16) Ohashi T, Arai Y, Ogasawara D: Therapeutic results after the introduction of tailored CAS. *JNET J Neuroendovascular Therapy* 2018; 12: 117–120.