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Overlap stenting for in-stent restenosis after carotid artery stenting

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ABSTRACT

Our aim was to assess the clinical safety and efficacy of overlap stenting for in-stent restenosis after carotid artery stenting. The study was conducted between July 2008 and February 2015. A database of consecutive carotid artery stenting procedures was retrospectively assessed to identify the cases of in-stent restenosis that were treated with overlap stenting under proximal or distal protection. The clinical and radiological records of the patients were then reviewed. Of the 155 CAS procedures in 149 patients from the database, 6 patients met the inclusion criteria. All the 6 patients were initially treated with moderate dilatation because of the presence of an unstable plaque. The technical success rate of the overlap stenting was 100%, with no 30-day mortality or morbidity. In addition, there was no further in-stent restenosis during a follow-up period of over 12 months. These results indicated that overlap stenting for in-stent restenosis after carotid artery stenting was both safe and effective in our cohort.

Key Words: carotid artery stenting, in-stent restenosis, retreatment

INTRODUCTION

In-stent restenosis (ISR) after carotid artery stenting (CAS) has been reported to be a relatively uncommon complication, with an incidence ranging from 2% to 8%.[1-7] Various treatment options have been reported for ISR, including additional balloon angioplasty, cutting balloons, and surgical stent removal; however, reliable evidence has not been established.[1-5] Donas *et al.* reported that balloon angioplasty for ISR after CAS required frequent repeat interventions.[1] Although they preferred balloon angioplasty alone to avoid narrowing the lumen with another stent, 5 of the 16 patients in that series suffered from recurrent ISR. To the best of our knowledge, the evidence for carotid artery overlap stenting has been limited to some case reports where it is described as a rescue procedure for acute in-stent thrombosis.[8] Therefore, we describe our clinical experiences when using overlap stenting for chronic ISR after CAS.

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MATERIAL AND METHODS

Study design

We performed a retrospective analysis of patients in a database of consecutive CAS procedures. Patients with ISR treated with overlap stenting under proximal or distal protection were included and their clinical data and outcomes were reviewed to assess the safety and effectiveness of the procedure. The study was conducted between July 2008 and December 2014, and results of follow-up examinations were obtained.

Patients

We collected data on all consecutive CAS procedures at our institution during the study period, including the details of the embolic protection device (EPD) used and whether open-cell or closed-cell stents were implanted. However, the present study focused only on those patients who developed ISR that was treated with overlap stenting. The clinical and radiological records of each patient was then obtained and retrospectively analyzed from electronic medical chart.

Procedures

1) Initial CAS strategy

All patients were placed on dual antiplatelet therapy with clopidogrel (75 mg daily) and either cilostazol (200 mg daily) or aspirin (100 mg daily) for at least 7 days before the CAS procedure. All procedures were performed under local anesthesia. The selection of the protection device and stent design depended on the findings on preoperative plaque images. If the images indicated a vulnerable plaque, we tended to choose a proximal balloon protection and a close cell stent. However, recently, proximal protection was selected whenever possible because it offered universal protection to most plaque lesions.[9-10)]

For the procedure, an 8-French gage (F) short sheath was introduced into the femoral artery. Intravenous heparin was then administrated to achieve an activated clotting time of 250¬–300 s. Our routine guiding system was co-axial with a 5-F inner catheter and an 8-F Optimo guiding catheter (TOKAI medical, Aichi, Japan). After advancing the Optimo guiding catheter into the common carotid artery, EPD was cautiously navigated under roadmap guidance to the distal lesion through the stenosis. Next, atropine sulfate (0.5 mg) was administered and pre-stenting balloon dilatation was most commonly applied to the narrowed lesions with a 3.5 mm × 40 mm angioplasty balloon.

The Carotid WALLSTENT® (Boston Scientific, Natick, MA, USA) was the most commonly deployed stent. Post-stenting dilatation was applied to the narrowest area using a 4.0–5.0 mm × 30 mm angioplasty balloon until 10 atmospheres of pressure or when the patient developed bradycardia. Postdilatation was cautiously performed and accepted up to approximately 50% residual stenosis. The dual antiplatelet therapy was continued for at least 30 days after CAS. Subsequently, single antiplatelet therapy with either clopidogrel (75 mg daily), cilostazol (200 mg daily) or aspirin (100 mg daily) was continued indefinitely.

2) Assessment and follow-up

Prior to CAS, patients underwent careful neurological examination, cerebral computed tomography, magnetic resonance imaging, carotid magnetic resonance angiography, echo/color-flow Doppler, and digital subtraction angiography. Follow-up with carotid ultrasound was typically after 3 days and after 1, 3, 6, 12, and 18 months. Digital subtraction angiography was performed when the flow velocity was 150 cm/s or more. Re-stenting (CAS) was indicated in symptomatic or asymptomatic patients with ISR of more than 50% or 80%, respectively. ISR was measured

according to the criteria of the North American Symptomatic Carotid Endoarterectomy Trial. If the stenosis did not meet these criteria, but was clearly deteriorating, only percutaneous transluminal angioplasty was performed.

3) Overlap CAS technique

Preoperative dual antiplatelet therapy and procedures of the guiding catheter placement were the same as those of the initial treatment. The inner membrane of ISR was believed to be formed by histologically stable intimal hyperplasia; therefore, the filter protection was used without hesitation, particularly in patients with apparent intolerance to transient internal carotid artery occlusion. As for the second stent (i.e., the overlap stent), we chose a longer stent than the first and placed it more distal to the first stent. After deploying the stent, post-stenting dilatation was applied to the narrowest area, using a 4.5–5.5 mm angioplasty balloons. Although postdilatation after the first CAS procedure was gently performed, this second postdilatation was strongly performed until the residual stenosis had been expanded to less than 30%.

RESULTS

Characteristics of overlap CAS

During the study period, 149 consecutive initial CAS procedures were performed at our institution (Table 1), among which 6 patients with ISR treated with overlap stenting were identified. The characteristics and outcomes of the 6 patients with ISR are summarized in Tables 2 and 3. All 6 patients were men, and their mean age was 72.5 years. Originally, 4 patients were symptomatic, and 5 patients had vulnerable plaques. The interval from initial treatment to retreatment was a median of 12 months (8–26 months). The average postoperative follow-up period after re-CAS was 19.2 months (12–32 months). Regarding the use of EPDs, initially, stenting balloon protections were used in all patients. At overlap stenting, filter protections were used in 3 patients. Although the lesions were easily crossed in 5 patients, the patient with the narrowest stenosis required additional predilatation. For the second stent (i.e., the overlap stent), we chose open-cell stents in 3 patients; in contrast, closed-cell stents were mainly used for the first stent. The residual stenosis after the initial and final treatments averaged 37% and 22%, respectively.

Table 1 Characteristics of CAS patients at initial stenting

		Total (n = 149)
Clinical presentation	Asymptomatic	51
	Symptomatic	98
Protection device	Distal filter	39
	Distal balloon	16
	Double balloon	94
Stent	Closed-cell stent	85
	Open-cell stent	64

Table 2 Clinical characteristics and perioperative findings at initial CAS in 6 patients by overlapping stent

Patient No.	Age	Sex	Clinical presentation	MRI plaque image	Plaque characterization	Initial stent	EPD at the initial CAS	Radiological findings	
								Residual stenosis at the initial treatment (%)	Post DWI high intensity spots after initial CAS
1	71	M	symptomatic	T1 high	vulnerable	WALL	Balloon	43	3
2	72	M	asymptomatic	T1 iso	not vulnerable	PRECISE	Balloon	47	1
3	70	M	asymptomatic	T1 high	vulnerable	WALL	Balloon	40	0
4	69	M	asymptomatic	T1 high	vulnerable	WALL	Balloon	43	0
5	83	M	symptomatic	T1 high	vulnerable	WALL	Filter (Contralateral ICA occlusion)	34	0
6	79	M	asymptomatic	T1 high	vulnerable	WALL	Balloon	13	1

CAS: carotid artery stenting
EPD: embolic protection device
DWI: diffusion weighted image
MRI: magnetic resonance imaging

Table 3 Interval to recurrence and perioperative findings before and after re-CAS treatment

Patient No.	Interval to recurrence (months)	Second stent	EPD at the second CAS	Ultrasound findings			Radiological findings	
				Pre-retreatment PSV of ICA	Post-retreatment PSV after 12 months	Significant re-restenosis after 12 months	Final residual stenosis (%)	Post DWI high intensity spots after second CAS
1	8	PRECISE	Balloon	388	96	NA	28	0
2	9	WALL	Filter	237	146	NA	25	0
3	15	PROTEGE	Balloon	231	79	NA	7	0
4	15	PRECISE	Filter	156	195	NA	25	3
5	8	WALL	Filter	309	98	NA	35	0
6	26	WALL	Balloon	178	50	NA	14	0

PSV: peak systolic velocity
NA: not applicable

Complications

There were no procedure-related complications in any of the 6 patients. The number of post-treatment magnetic resonance diffusion-weighted image spots the day after treatment was 0–3 (median 0, mean 0.5). Owing to the limited ischemic complications, no patient developed new neurological symptoms during the perioperative period, and there was no 30-day mortality or morbidity. Although only case 4 showed a little worsening of ICA velocity 12 months after overlap stenting, there was no further ISR during the follow-up period of over 12 months (Table 3).

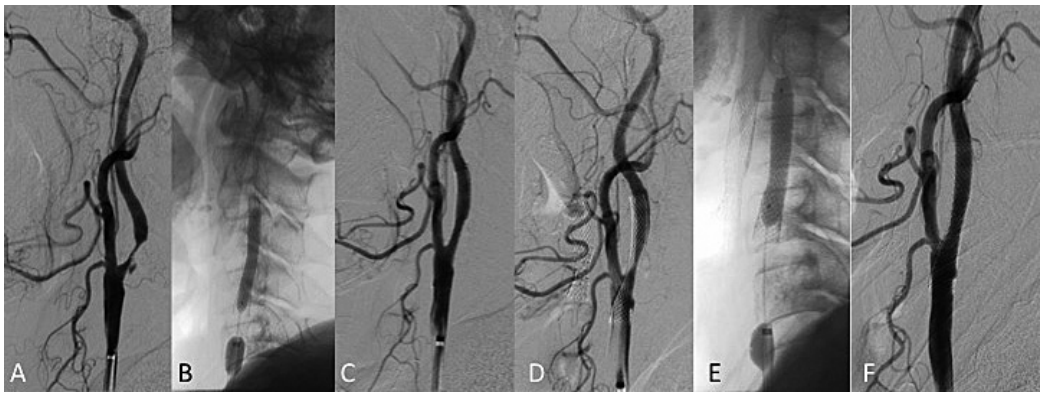

Fig. 1 Lateral angiography images of initial CAS and re-CAS procedures in case 1

Fig 1A: Initial digital subtraction angiography (lateral view) showed severe stenosis and ulcerous change of the left internal carotid artery.

Fig. 1B: Postdilatation was performed using a 4.0 mm × 30 mm balloon under double balloon protection.

Fig. 1C: Final view after deployment of the first stent (Carotid WALLSTENT® 8.0 mm × 21 mm).

Fig. 1D: Digital subtraction angiography revealed in-stent restenosis.

Fig. 1E: Postdilatation was applied aggressively with a 4.5 mm × 30 mm angioplasty balloon under distal filter protection during the second (overlap) stenting procedure.

Fig. 1F: Final view after the second (overlap) stenting (PRECISE® 8.0 mm × 30 mm).

A representative case

A representative case can be seen in Figures 1A–F. The case is of a man in his early seventies who presented with acute ischemic symptoms. Originally, severe stenosis was evident bilaterally in his internal carotid arteries. The first balloon percutaneous transluminal angioplasty was gently performed in the right internal carotid artery before left-sided CAS was performed (Figure 1A–C). A few months later, the carotid stent was deployed as the second stage of treatment for the right side lesion. However, 8 months after the left-side CAS, ultrasound revealed ISR with a maximum velocity of 388 cm/s in the left internal carotid artery. Digital subtraction angiography showed severe ISR (Figure 1D), so overlap stenting was deployed with aggressive postdilatation using a larger angioplasty balloon (Figures 1E and F).

DISCUSSION

In the present study, we have summarized our experience of overlap stenting for chronic ISR after CAS, including a detailed review of a representative case. We assessed the clinical safety and efficacy of overlap stenting for ISR after CAS. Concurrently, the risk factors and period of developing ISR showed a similar trend with those of previous reports.

Most ischemic events in patients with carotid artery stenosis initially tend to have an embolic source and are not related to chronic hypo-perfusion.[8] The initial CAS procedure should be performed to prevent future embolization by scaffolding the ruptured plaque against the vessel wall using a stent, avoiding intra-procedural plaque rupture if possible. Greater degrees of postdilatation are associated with more scissoring of the stent wires on the plaque that eventually leads to embolization. As for stent, Bosiers *et al.* reported that closed-cell stents had lower postprocedural complication rates than open-cell stents.[7] Therefore, we employed gentle postdilatation and closed-cell stents at the first stenting for vulnerable plaque as a secure method.

Table 4 Published reports regarding ISR after CAS in the recent decade and our series.

Author	Case number	ISR rate	Endovascular treatment				Recurrence
			BA	CB	BA + Stent	Surgery	
Setacci 2005 [3]	15/416	3.6%	3	4	8		0
Levy 2005 [2]	6/122	4.9%	4	1	1		2
Zhou 2006 [4]	7/208	3.4%	1	4	2		2
Reimers 2006 [18]	32/820	3.2%	12	10	10		1
Donas 2011 [1]	16/482	3.3%	12	0	1	3	5
Current study 2015	6/149	4.0%	0	0	6		0

BA: Balloon Angioplasty
CB: Cutting Balloon

Table 4 shows the summary of treatment for ISR previously described in the literature (surgical stent removal is included). Generally, because the intimal hyperplasia that is recognized as a major cause of ISR comprises fibrous tissue with smooth muscle cell proliferation, additional interventions, such as PTA or overlap stent, are safe and have little risk of plaque rupture.[11] All our patients were successfully treated with overlap stenting without any thromboembolic complications despite that fact that we used a larger postdilatation balloon and permitted the use of open-cell stents that have stronger radial force than closed-cell stents in the second procedure, regardless of whether patients had vulnerable plaques. Among these reports, Donas *et al.*[1] and Levy *et al.*[2] selected balloon angioplasty in more than half of the cases, and their recurrence rates were relatively frequent compared with those of other series. Compared with it, none of our patients showed any recurrence after overlapping stent for an average of 19.2 months.

As shown in our study (Table 2), it is possible that residual stenosis greater than about 30% after the initial treatment could be a risk factor for restenosis. Shankar *et al.* also reported that the most important factors associated with restenosis were residual stenosis of more than 30% (particularly ≥50%) in the immediate post-CAS period and a plaque length of more than 2 cm.[12] Ogata *et al.* similarly commented that residual stenosis of 30% or more was significantly associated with restenosis or subacute stent thrombosis.[6] Specifically, the risk of restenosis appeared greatest when gentle postdilatation resulted in a residual stenosis of 30% or more among patients with unstable plaques. When ISR occurs, intimal hyperplasia typically follows 3 months to 3 years after initial CAS.[13-15] In our series, ISR also arose at a median of 12 months. It is necessary to recommend close follow-up examinations to patients with residual stenosis, as per our hospital protocol.

This report has some limitations. Of note, we only included a small number of patients with ISR from a single institution in a retrospective design. Therefore, we were also unable to compare different treatment options, such as cutting-balloon angioplasty, drug-eluting balloons, or surgical stent removal. The careful observation of the course of patients undergoing overlap stenting will be required to evaluate the long-term durability and prognosis associated with the procedure. Further case collection and reporting are therefore required.

CONCLUSIONS

Our results indicated that overlap stenting for ISR after CAS was both safe and effective.

However, further large-scale, prospective, multi-center studies are required to confirm our findings.

CONFLICT OF INTEREST DISCLOSURE

The authors declare that there is no conflict of interest.

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