Original Article

Calcification in original plaque and restenosis following carotid artery stenting

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Abstract

Background: The relationship between calcification in primary plaque and recurrent stenosis after carotid artery stenting (CAS) is not established, but an inverse association with restenosis following carotid endarterectomy (CEA) has been suggested.

Methods: We retrospectively analyzed 75 plaques of 109 consecutive CAS with regard to calcification, using the calcium score and shape, location, and other characteristics of original plaques together with stenting-related factors. CAS was performed in a standard fashion with an embolic protection device. Greater-than-moderate restenosis ($\geq$ 50%) was assessed by peak systolic velocity (PSV) with duplex ultrasonography ($\geq$ 130 cm/s, internal/common carotid or distal/proximal PSV ratio $\geq$ 2.0).

Results: Univariate analysis revealed percentages of dyslipidemia treated with statins ($P = 0.03$), calcification in distal ICA ($P = 0.02$), and immediate residual stenosis ($P = 0.02$) were significantly higher in patients with greater-than-moderate restenosis, whereas calcification in carotid bulb and usage of open-cell stent were rather less frequent ($P < 0.001$ and $P = 0.02$, respectively). Multivariate logistic regression analysis showed that rarity of calcification in carotid bulb was a sole independent predictor for greater-than-moderate recurrent carotid stenosis 1 year after CAS (OR = 0.21, CI = 0.06–0.77, $P = 0.02$).

Conclusions: Calcium score was not significantly related to restenosis at 1 year after CAS, as was previously found following CEA, though scarcity of calcification in carotid bulb was suggested as a predictor of in-stent restenosis. Compared to post-CEA restenosis, carotid plaque calcification may be inversely but tenuously associated with recurrent stenosis 1 year post-CAS. No other stenting factors (e.g., stent design, pre-/post-dilation, or protection devices) showed a significant association with recurrent stenosis post-CAS.

INTRODUCTION

Recurrent stenosis or in-stent restenosis after carotid artery stenting (CAS) is known as a risk factor of ipsilateral stroke, and this stroke risk should be monitored during patient follow-up.[22–24] Several factors related to post-CAS restenosis have been reported, including demography, comorbidity, and/or characters of original plaques, e.g., age,[4,22] female gender,[22] symptomatic cases,[13] diabetes,[5,22] hypertension,[22,40] hyperlipidemia,[22] inflammation markers,[37] high-degree stenosis,[32] and length of the plaques,[31] although some of these studies merely conducted univariate or combined analyses with restenoses after carotid endarterectomy (CEA). Several researchers reported CAS-procedure-related factors of post-CAS restenosis, such as immediate residual stenosis,[7,31,40] double stent deployment,[7] use of an open-cell stent,[20] and the predilation balloon diameter.[32]

A recent research clarified that greater-than-moderate recurrent stenosis after CEA was less frequent in carotid plaques with higher calcium scores, indicating that plaque calcification is inversely related to post-CEA restenosis.[15] However, the mechanism of restenosis that occurs within a few years after CAS is thought to be due to myointimal hyperplasia, as in CEA, whereas the mechanism of later post-CAS stenosis is thought to be due to atherosclerosis.[7] If the post-CAS etiology is similar to that of post-CEA restenosis in the early period, it is conceivable that there is an analogous association between calcification in carotid plaque and recurrent stenosis; however, the relationship between plaque calcification and restenosis after CAS has not been thoroughly investigated. We conducted the present study to evaluate the calcification in original plaque using the calcium score as well as the shape and location of the plaque, and to elucidate the involvement of these and other factors in the recurrence of stenosis after CAS.

PATIENTS AND METHODS

Patient population and surgical treatments

The sample included a total of 109 consecutive cases of CAS performed between February 2005 and December 2015. Fifteen patients with follow-up periods <1 year, seven patients with secondary stenting, 11 patients with missing peak systolic velocity (PSV) data of duplex ultrasonography (DUS) at 1 year, and two patients without computed tomography angiography (CTA) data for renal failure were excluded from the study. A final total of 75 carotid arteries with CAS including two bilateral stentings and four post-CEA cases were enrolled in the study and retrospectively analyzed. The mean follow-up period was 43.3 ± 29.5 months. No transient or permanent focal neurologic symptoms of the contralateral limbs or ipsilateral retina were observed in the patients with postoperative recurrent stenosis. The patient data are summarized in Table 1.

Surgical indications for the treatment of carotid stenosis adhered to the criteria of the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[6] the Asymptomatic Carotid Atherosclerosis Study (ACAS),[1] and the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE)

Table 1: Characteristics of cases stratified according to degree of stenosis at 1 year

Degree of restenosis at 1 year post-operation (%)	Total	0 ≤stenosis <50	≥50 stenosis*	*P*
n	75	55	20	-
Age (yr/o)[a]	73.8±7.0	74.5±6.8	71.7±7.4	0.12
Male sex (%)[b]	81.3	81.8	80.0	0.75
Degree of original carotid stenosis (%)[a]	77.7±14.2	76.7±15.0	80.8±11.9	0.28
Symptomatic case (%)[b]	72.0	72.7	70.0	0.28
Follow-up period (day)[a]	1314.0±893.7	1280.8±920.3	1405.3±831.8	0.45
Antihypertensive use (%)[b]	68.0	67.3	70.0	0.68
Hypoglycemic drug use (%)[b]	37.3	34.5	45.0	0.13
Statin use (%)[b]	76.0	72.7	85.0	**0.03**
Ischemic heart disease with PCI (%)[b]	17.3	16.4	20.0	0.51
Renal malfunction (%)[b]	4.0	5.5	5.0	0.87
Smoking history (%)[b]	45.3	47.3	40.0	0.30
Antiplatelet use (%)[b]	100.0	100.0	100.0	-
Anticoagulant use (%)[b]	6.7	7.3	5.0	0.50

[a]Mann-Whitney U-test, [b]Chi-square analysis. PCI: Percutaneous coronary intervention, *PSV: Peak systolic velocity ≥130 cm/sec, internal/carotid artery or distal/proximal PSV ratio ≥2.0

study.[38] The surgical methods and selection of CAS and CEA were as described.[17,19] CAS was performed using a Wallstent® in 44 of the 75 cases (58.7%) (Boston Scientific, Freemont, CA) and a PRECISE® stent in the other 31 cases (41.3%) (Cordis, Bridgewater, NJ,) with or without predilation (6 atm, 30 s, Sterling®, Boston Scientific) and postdilation (10 atm, 10–15 s, Aviator®, Cordis). A filter (Angioguard XP®, Cordis), distal balloon (PercuSurge® Guardwire, Medtronic, Santa Rosa, CA), and/or flow reversal (Patlive®, Terumo Clinical Supply, Kakamigahara, Japan) embolic protection devices were used.

The use of pre-/postdilation and the selection of the types of stents and protection devices were determined at the discretion of the interventionalists. Dual antiplatelet therapy (DAPT) using mainly aspirin (100 mg/day)/ clopidogrel (75 mg/day) or cilostazol (200 mg/day) were performed (except in six cases with a clopidogrel/ cilostazol combination and two with triple antiplatelet therapy) at ≥5 days before CAS and were continued after the procedure for 3 months; and a lifetime continuation of solely aspirin was prescribed.

The patients' use(s) of antihypertensives, hypoglycemic drugs, statins, antiplatelets, and anticoagulants were checked. Renal malfunction was defined as serum creatinine >1.5 mg/dl and/or blood urea nitrogen (BUN) >30 mg/dl. History of smoking was defined as a patient who had a pattern of >100 cigarettes/lifetime in the past and/or at the time of recording.

The study design was approved by the local ethics committee, and the ethical guidelines for medical and health research involving human participants issued by the Japanese Health Labor and Welfare Ministry (2014) were strictly observed.

Assessment of the calcium score of the plaques with multidetector row computed tomogaphy

Multidetector row CT (MDCT) angiography was performed preoperatively in all enrolled patients with a 64-detector row CT scanner (SOMATOM Definition: Siemens Medical Solutions, Forchheim, Germany) or a 16-detector row CT scanner (IDT-16: Philips Medical Systems, Best, Netherlands).[17,18] The imaging acquisition parameters were as follows: spiral mode 0.33-s gantry rotation; collimation, 32×0.6 mm; pitch factor, 1.5; section thickness 1.0 mm; reconstruction interval, 0.5 mm, and acquisition parameters 120 kVp and 350 mA. A total of 50 ml of nonionized contrast medium [either iohexol (Omnipaque 300; Daiichi Sankyo, Tokyo) or iopamidol (Iopamiron 300; Bayer Schering Pharma, Berlin, Germany)] was injected at a flow rate of 3.5 ml/s, followed by a 25-ml saline chaser at the same rate as the contrast medium.

The optimal timing of MDCT angiography acquisition was determined by an automated bolus-timing program.

Images were obtained from the aortic arch to the level of the inferior orbits. The image data were transferred to a computer workstation (Ziostation version 1.17; Amin, Tokyo) for image postprocessing, and the calcification of the carotid plaque was preoperatively quantified. The Agatston calcium score[3] of any calcification area >1 mm^2 with attenuation ≥130 Hounsfield units (HU) was determined by multiplying the lesion area (total number of pixels) by the cofactor 1–4 (cofactor 1, 130–199 HU; cofactor 2, 200–299 HU; cofactor 3, 300–399 HU; cofactor 4, ≥400 HU) with noncontrast-enhanced CT obtained before the contrast media injection for CT angiography. Calcium was further quantified in cubic millimeters with the volume score calculated as the product of the voxel volume and the number of voxels in the region of interest; the overall calcium score of the plaque was the sum of the values for all individual lesions by computer-assisted automatic measurement.

Assessment of the calcification in carotid plaque, positive remodeling, and stenosis

Assessment of plaque calcification characteristics was preoperatively performed as described.[16] The shape of the calcification in the carotid plaque was stratified and scored with enhanced MDCT according to "circularity," or the degree to which the plaque encircled the vessel perimeter: 1, less than one-quarter; 2, one-quarter to one-half; 3, more than one-half up to three-quarters; 4, more than three-quarters up to less than a full circle; and 5, full circle covering the entire carotid perimeter.

We classified and scored the inner (intimal) and outer (adventitial) position of the calcification in the carotid plaque in the carotid wall based on enhanced CT: 1, inner side in the carotid wall only; 2, inner >outer, 3: inner = outer, 4: inner <outer, 5: outer side in the carotid wall only. The location of plaque calcification was assessed in terms of whether calcification existed in the common carotid artery (CCA), the bulb, and/or the distal part of the internal carotid artery (ICA), allowing multiple registries.

We determined the degree of pathological findings other than calcification based on histopathological specimens of the extracted plaques stained with hematoxylin-eosin just after the operation and scored as follows: lipid core (0: none, 1: small, 2: medium, 3: large), fibrous tissue (0: none, 1: thin, 2: thick), and intraplaque hemorrhage (0: none, 1: slight, 2: prominent).

Positive remodeling was defined as a remodeling ratio (RR) >1.1, where RR = the cross-sectional diameter (CSD) at the point of maximum stenosis in the (ICA)/the reference CSD at the distal ICA.[28] The height of the distal end of the carotid plaque was divided when it existed beyond the level over C2. The location of the restenosis was evaluated with respect to whether

stenosis existed in the proximal CCA, the CCA to carotid bulb, and the ICA to the carotid bulb and/or distal ICA, allowing multiple registries.

Assessment of the stenting-related factors

The stent types (open-/closed-cell), implementation of pre-dilation/post-dilation, and protection for embolization (distal/proximal) were checked and evaluated. Carotid tortuosity was defined as carotid curvature of the stenting site <120°, and a difficult distal landing zone was determined as severe angulation or tortuosity for protective embolic devices, according to the Buffalo risk assessment scale (BRASS).[11]

Duplex ultrasonography

The degree of restenosis after CAS was assessed by PSV on high-resolution ultrasonography, with a linear transducer at 7.5 MHz in the B mode (Aplio, Toshiba Medical Systems, Otawara, Japan). The highest PSV from the treated ICA or CCA was used to identify restenosis. The PSV threshold for predicting ≥50% carotid stenosis was 130 cm/s based on a recent precise study[35] plus a PSV ratio ≥2.0 for the ICA to the CCA or the distal to proximal portion of the stenosis. The minimal diameters of the greater-than-moderate restenoses (≥50%) were all ≤3.0 mm.

Statistical analysis

All statistical evaluations were performed with Statview ver. 5.0 software (SAS, Cary, NC) and StatMate III (ATMS, Tokyo), and all results are presented as mean ± SD values. The Chi-square test with Yates' correction and the Mann–Whitney U-test were used for comparisons. For the multivariate analysis, a binary logistic regression model was used. Probability (P) values <0.05 were considered significant.

RESULTS

Baseline characteristics

There were no significant differences in basic data concerning age, gender, degree of original carotid stenosis or follow-up period between the groups with no-or-mild stenosis (<50%; n = 55) and greater-than-moderate restenosis (≥50%; n = 20) groups at 1 year postoperation [Table 1]. The percentage of patients with dyslipidemia treated with a statin was significantly higher in the greater-than-moderate restenosis group at 85% compared to the no-or-mild stenosis group at 72.7% (P = 0.03). The use of antihypertensives or several other important drugs and smoking habit were not significantly different between the two groups.

Original plaque characteristics and factors for stenting

We performed a univariate analysis for the above two groups regarding original plaque characteristics. No significant difference was found for the length, height of the distal end, positive remodeling, or location of the initial stenosis [Table 2]. Regarding calcification in the carotid plaques, in the greater-than-moderate restenosis group, calcification's existence was significantly less frequent in the carotid bulb but significantly more frequent in the distal ICA compared to the other group (P < 0.001 and P = 0.02, respectively). There were no significant differences in

Table 2: Characteristics of plaque and stenosis stratified according to degree of stenosis at 1 year

Degree of restenosis at 1 year post-operation (%)	Total	0 ≤stenosis <50	50 ≤stenosis*	P
Original plaque length (mm)[a]	24.0±9.3	23.7±9.3	25.0±9.1	0.74
Original plaque distal end: C2 or upper (%)[b]	38.7	40.0	35.0	0.47
Original plaque (stenosis) location[b]				
CCA-bulb (%)	28.0	30.9	20.0	0.36
ICA-bulb (%)	84.0	81.8	90.0	0.10
Distal ICA (%)	22.7	25.5	15.0	0.06
Positive remodeling (%)[b]	20.0	18.2	25.0	0.24

[a]Mann-Whitney U-test, [b]Chi-square analysis. CCA: Common carotid artery, ICA: Internal carotid artery. *PSV: Peak systolic velocity ≥130 cm/sec, internal/carotid artery or distal/proximal PSV ratio ≥2.0

Table 3: Characteristics of plaque and stenosis stratified according to degree of stenosis at 1 year (regarding calcification)

Degree of restenosis at 1 year post-operation (%)	Total	0 ≤stenosis <50	50 ≤stenosis*	P
Calcium score[a]	314.0±395.4	330.5±417.6	268.7±332.0	0.65
Calcification shape score (circularity)[a]	1.5±1.1	1.5±1.1	1.5±1.3	0.74
Calcification position score (inside/outside)[a]	2.3±2.0	2.3±2.0	2.3±2.0	0.71
Calcification location[b]				
CCA (%)	48.0	50.9	40.0	0.12
Carotid bulb (%)	65.3	72.7	45.0	**<0.001**
Distal ICA (%)	20.0	16.4	30.0	**0.02**

[a]Mann-Whitney U-test, [b]Chi-square analysis. *PSV: Peak systolic velocity ≥130 cm/sec, internal/carotid artery or distal/proximal PSV ratio ≥2.0

calcium score, calcium shape score (circularity), or position score (inside/outside) between the two groups [Table 3].

Concerning the stenting-related factors, the use of an open-cell stent was significantly less frequent in the greater-than-moderate restenosis group, whereas immediate residual stenosis was significantly higher (both $P = 0.02$) by univariate analysis. No significant differences between the no-or-mild and greater-than-moderate restenosis groups were revealed concerning pre- and post-dilation, the use of proximal embolization protection, carotid tortuosity, and difficult distal landing zone [Table 4].

The results of the multivariate logistic regression analysis indicated that scarce calcification in the carotid bulb was the only significant independent predictor of post-CAS greater-than-moderate restenosis at 1 year (OR = 0.21, CI = 0.06–0.77, $P = 0.02$) [Table 5]. The pictures of representative cases are shown in Figures 1–4.

Table 4: Stenting-related factors stratified according to degree of stenosis at 1 year

Degree of restenosis at 1 year post-operation (%)	Total	0 ≤stenosis <50	50 ≤stenosis*	P
Open-cell stent (%)	41.3	45.5	30.0	**0.02**
Pre-dilation (%)	92.0	90.9	95.0	0.39
Post-dilation (%)	56.0	58.2	50.0	0.75
Proximal embolization protection (%)	45.3	47.3	40.0	0.30
Carotid tortuosity[a] (%)	8.0	7.3	10.0	0.67
Difficult distal landing zone[b] (%)	4.0	3.6	5.0	0.89
Immediate residual stenosis (%)	20.0	16.4	30.0	**0.02**

Chi-square analyses. *PSV: Peak systolic velocity ≥130 cm/sec, internal/carotid artery or distal/proximal PSV ratio ≥2.0. [a]Carotid curvature of the stenting site <120°. [b]Severe angulation/tortuosity for protective embolic devices
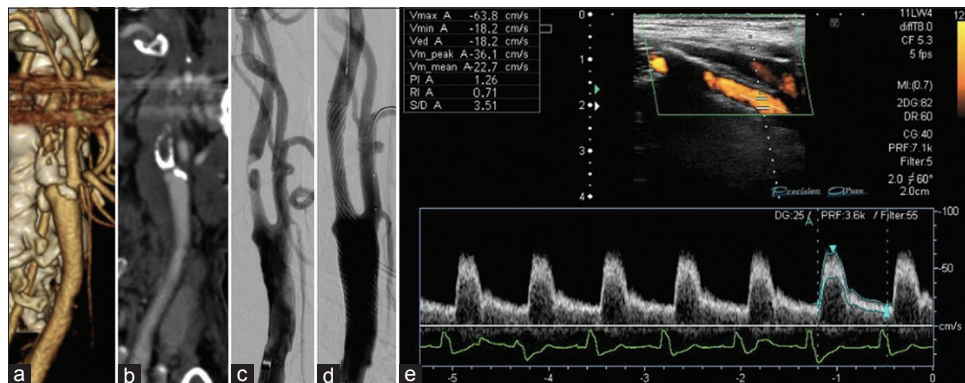
Figure 1: A 84-year-old male with right asymptomatic carotid stenosis. Volume rendering (a), maximum intensity projection (b), images of multidetector row CT and digital subtraction angiography (c), before carotid artery stenting (CAS). Calcification was observed in the carotid bulb and the common carotid artery. (d) The Wallstent® was successfully placed immediately after the procedure. (e) Duplex ultrasonography one year after CAS revealed that the peak systolic velocity was 63.8 cm/s
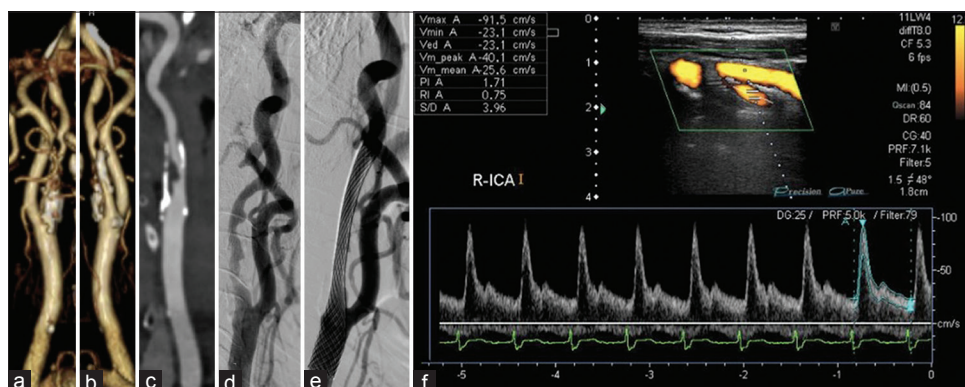
Figure 2: A 81-year-old male with right symptomatic carotid stenosis. Volume rendering (a, b) maximum intensity projection (c), images of multidetector row CT, and digital subtraction angiography (d) before carotid artery stenting (CAS). Calcification was observed in the carotid bulb, the common and distal internal carotid artery. (e) The Wallstent® was successfully placed immediately after the procedure. (f) Duplex ultrasonography one year after CAS revealed that the peak systolic velocity was 91.5 cm/s
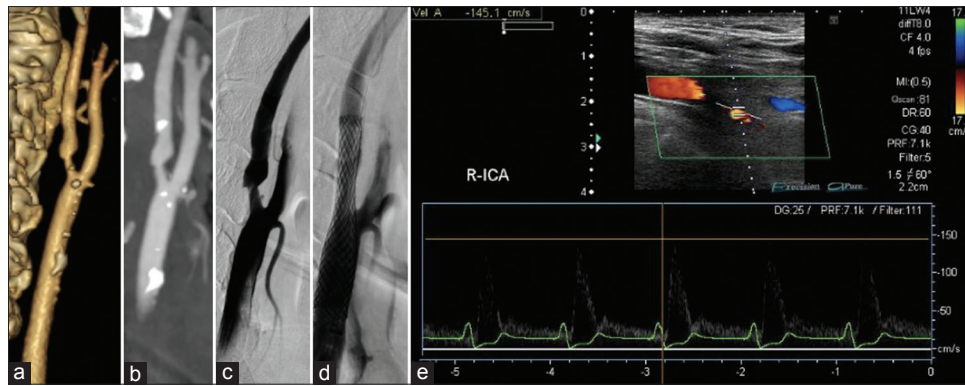
Figure 3: A 73-year-old male with right symptomatic carotid stenosis. Volume rendering (a), maximum intensity projection (b), images of multidetector row CT and digital subtraction angiography (c), before carotid artery stenting (CAS). Calcification was observed in the common and the distal internal carotid artery. (d) The Wallstent® was successfully placed immediately after the procedure. (e) Duplex ultrasonography one year after CAS revealed that the peak systolic velocity (PSV) was 145.1 cm/s and the PSV ratio for the distal to the proximal portion of the stenosis was 2.0
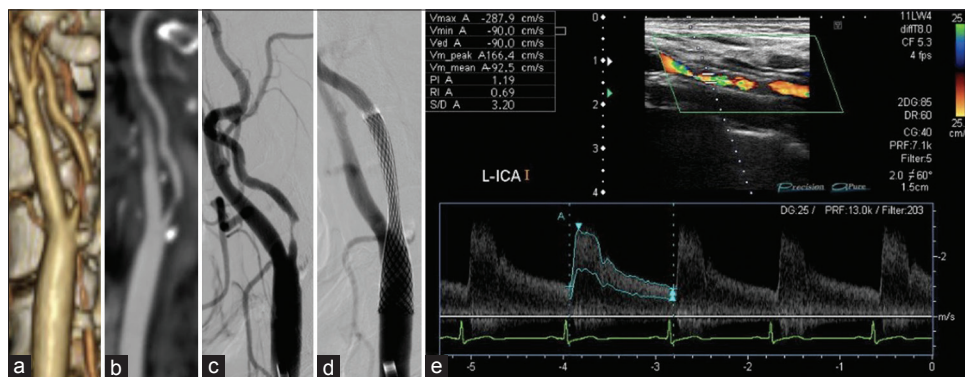
Figure 4: A 65-year-old male with left symptomatic carotid stenosis. Volume rendering (a), maximum intensity projection (b), images of multidetector row CT and digital subtraction angiography (c), before carotid artery stenting (CAS). Calcification was observed only in the common carotid artery. (d) The Wallstent® was successfully placed immediately after the procedure. (e) Duplex ultrasonography one year after CAS revealed that the peak systolic velocity was 287.9 cm/s and the PSV ratio for the distal to the proximal portion of the stenosis was 6.1

Table 5: Multivariate logistic regression analysis of greater-than-moderate postoperative restenosis at 1 year*

|	Odds ratio	95% CI	*P*
Age (<71)	1.20	0.33-4.37	0.79
Female sex	1.58	0.36-6.95	0.54
Treated dyslipidemia	2.77	0.57-13.6	0.21
Calcification on carotid bulb	0.21	0.06-0.77	**0.02**
Calcification on distal ICA	1.48	0.34-6,44	0.60
Open-cell stent	0.42	0.11-1.65	0.21
Immediate residual stenosis (>50%)	1.64	0.42-6.36	0.48

*PSV: Peak systolic velocity ≥130 cm/sec, internal/carotid artery or distal/proximal PSV ratio ≥2.0

DISCUSSION

Our study's multivariate regression analysis revealed that scarcity of calcification in the carotid bulb was the sole independent predictor of greater-than-moderate recurrent stenosis after CAS. The calcium score and the calcification circularity, which have been reported to be predictors of restenosis in CEA,[15] were not significant in the relationship between calcification and post-CAS restenosis in the present study.

Comparison of the present and previous findings regarding restenosis after CAS

Prior investigations of restenosis after CAS showed several important and related factors concerning demographics and comorbidity. As a large study, a subanalysis of the CREST trial[22] revealed that female gender, diabetes, and dyslipidemia were independent predictors of restenosis or occlusion after CEA and CAS. A subanalysis of the EVA-3S study[4] showed that restenosis (≥50%) or occlusion was significantly higher after CAS than after CEA, and that the patient's age at baseline was the only vascular risk factor. Recent studies described diabetes,[5,30] a history of cerebrovascular disease, and having a cerebrovascular accident prior to stenting,[9] smoking, symptomatic stenosis, and *de-novo* stenosis[30] as predictors of in-stent recurrent stenosis. Zapata-Arriaza *et al.*[40] reported that hypertension and impaired vasoreactivity were independent risk predictors of restenosis (≥70%), though their cohort included

only angioplasty cases without stents. Regarding characteristics of the original plaque, plaques longer than 20 mm were reported to be significantly related to restenosis.[31]

In our present study, we found no significant difference between the no-or-mild restenosis and greater-than-moderate restenosis groups concerning demographics, concomitant conditions, and characteristics of the original plaque and stenosis [Tables 1 and 2] except for statin use. Some experimental reports described that statins were effective for counteracting restenosis, but this has not been confirmed.[14,33] AbuRahma *et al.* reported that statins had no effect on preventing post-CEA restenosis, although statins lowered the postoperative death and stroke rates in diabetic patients.[2]

Regarding the usage of antiplatelets, several reports indicated a therapeutic effect of cilostazol.[26,34,39] In the present study, the rate of prescriptions of cilostazol showed no significant difference between the no-or-mild restenosis and greater-than-moderate stenosis groups: 52.7% (29/55) vs. 50.0% (10/20), respectively.

Relationship between restenosis and factors related to CAS

Regarding the factors related to stent materials, procedures, and the postoperative state, the reported independent predictors of restenosis are immediate post-CAS residual stenosis,[7,31] stent length and width,[37] and double stent deployment.[7] Plaque protrusion has been reported to be observed frequently in open-cell stent use compared to closed-cell stents,[20] but de Donato *et al.*[10] demonstrated that stent characteristics (material/design/free-cell area) were not significantly associated with in-stent restenosis in a 5-year follow-up. Okahara *et al.* also showed no difference in plaque protrusion between open- and closed-cell stents.[29]

In our study, though the multivariate analysis revealed no significance, the results of the univariate analysis regarding immediate residual stenosis was in accordance with previous reports,[7,31] although open-cell stent use was rather less frequent in the present greater-than-moderate restenosis group. This might be related to the variations among the studies regarding the definition of restenosis and the modalities used to assess the degree of restenosis and its definition, especially the estimated degree of stenosis and the corresponding PSV in DUS as was suggested.[8] The discordant findings might also have been affected by the limited number of samples in the present study.

Calcification in carotid plaques and restenosis after CAS

Concerning calcification in original plaque, Moon *et al.*[27] reported that calcification might be a predictor of

restenosis (≥50%), though their follow-up period varied from 1 to 204 months. In addition, they did not describe how they evaluated calcification and what type of stents they used. Ronchey *et al.*[30] showed that calcification was associated with restenosis as well as other factors based on their analysis of 1,000 cases of CAS using Wallstents®. Although they defined plaques with Gray-Weale classifications III/IV[12] as calcified plaques, those classes actually contained fibrous plaques as echogenic carotid plaques.

On the other hand, Wasser *et al.*[36] speculated that the risk of intima injury (which is suspected to be the initial trigger of restenosis) was lower in calcified plaques compared to soft vulnerable plaques. Misaki *et al.*[25] recently reported that a high volume of plaque components with radiodensities <0 HU was independently associated with the increased risk of restenosis after CAS.

Here, we used a calcium score that was an integrated indicator encompassing hardness and volume. We also precisely evaluated the calcification, i.e., its shape, position, and location. However, scarcity of calcification in the carotid bulb was the sole independent predictor by multivariate analysis. The incidence of the greater-than-moderate restenosis that occurred in the area concerning the carotid bulb for plaques without calcification (9/11; 81.8%) was greater than that for plaques with calcification in the same area (33.3%; 3/9). This suggests that calcification was inversely associated with restenosis, which is in line with the findings reported by Misaki *et al.*

A previous analysis concerning restenosis after CEA revealed an apparent inverse relationship with a calcium score and the circularity of calcification,[15] and our present results demonstrated that in-stent restenosis following CAS was also inversely but tenuously associated with calcification in carotid plaques compared to that in CEA. The reason for this modest association is obscure, but it might be ascribed to multiple complex factors and their interactions such as plaque protrusion/thrombus, stent materials, and stenting techniques (which would not be expected to be associated with CEA) though they may not have intimate involvement in restenosis individually.

Limitations

The primary limitations of our study are its retrospective character and the small number of cases. We used DUS for the assessment of the degree of in-stent restenosis, whereas the use of PSV to estimate the degree of stenosis varies among researchers.[8,35] Though DUS was avoided and CTA was used for the study of restenosis after CEA,[15] CTA was reported to overestimate the percent stenosis for beam-hardening artifacts and was inferior to DUS in determining in-stent restenosis.[21] We used DUS in the present study, but it is possible that our study included cases of milder restenosis than those examined

in other studies, although we applied the criteria from a recent meticulous study.[8,35]

CONCLUSIONS

Scarcity of calcification in the carotid bulb was the sole predictor of in-stent restenosis 1 year after CAS, and the calcium score was not significantly associated with recurrence, as was observed following CEA. The relationship between carotid calcification and recurrent stenosis 1 year after CAS might be reverse, but it may be more tenuous than that after CEA.

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