ORIGINAL RESEARCH

Optical coherence tomography evaluation of tissue prolapse after carotid artery stenting using closed cell design stents for unstable plaque

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ABSTRACT

Background and purpose During carotid artery stenting (CAS) with the use of closed cell design stents for unstable plaques, tissue prolapse between stent struts was evaluated by optical coherence tomography (OCT).

Methods 14 carotid stenosis lesions diagnosed as unstable plaques by MRI were evaluated by OCT imaging during CAS using closed cell stents. Cross sectional OCT images within the stented segment were evaluated at 1 mm intervals. The slice rate for the presence of tissue prolapse between the struts was calculated.

Results No intra-procedural complications occurred. After single stent placement, tissue prolapse was observed in all cases. Slices with any and >500 μm tissue prolapse were seen in 30% and 7.8% of cases, respectively. In 5 of 7 lesions with tissue prolapse >500 μm, additional stents were overlapped. In cases with overlapping stents, slices with any tissue prolapse were significantly decreased from 26% to 16% (p=0.008); in particular, the occurrence of tissue prolapse >500 μm was significantly decreased from 15% to 2.3% (p<0.001). In one case of >500 μm tissue prolapse without an overlapping stent, delayed embolization due to an in-stent thrombus occurred 9 months after the procedure.

Conclusions OCT during CAS using closed cell stent for unstable plaques frequently revealed tissue prolapse between struts. Placement of overlapping stents significantly reduced tissue prolapse, particularly tissue prolapse >500 μm. However, closed cell stents used for unstable plaques may not solve the problem of tissue prolapse.

INTRODUCTION

Atherosclerotic carotid artery stenosis is a main cause of cerebral stroke. Carotid artery stenting (CAS) has emerged as a therapeutic alternative to carotid endarterectomy (CEA) for the treatment of carotid artery stenosis; however, the rate of ischemic complications for CAS is higher than for CEA.¹ CAS for unstable plaques presents a high risk of ischemic complications; therefore, protective devices such as a distal filter or proximal protection system have been developed to prevent intra-procedural ischemic events,² and stents with a closed cell (CC) design have been applied.³

Plaque prolapse between stent struts after CAS can occur and causes delayed ischemic embolization.⁴ CC stents have low adaptability to vessels and low cell size areas; therefore, the possibility for plaque prolapse to occur is less and they are frequently used during CAS for unstable plaques.⁵ However, conventional intra-vascular ultrasound (IVUS), ultrasound, and CT cannot clearly detect plaque prolapse during CAS and follow-up periods.

Optical coherence tomography (OCT) is a progressively accepted intravascular modality for studying coronary arteries. It provides unprecedented microstructural information regarding atherosclerotic plaques and placed stents, and has a high resolution capacity of 10 μm. OCT has been used to assess atherosclerotic carotid plaque morphology, tissue prolapse, and stent apposition. Its safety and feasibility for use with carotid arteries have been reported recently.⁶⁻¹² To date, limited information has been available regarding the complex interaction between carotid plaques and stents because neither angiography nor IVUS has the microscale resolution capable of identifying such imperfections.

The aim of this study was to use OCT to detect and evaluate tissue prolapse between stent struts during CAS using CC stents for unstable plaques.

MATERIALS AND METHODS

From January 2015 to June 2016, carotid revascularization was performed for 88 lesions in 85 patients at our hospital. CEA was performed for 25 lesions in 25 patients, and CAS was performed for 63 lesions in 60 patients. CEA was mainly performed for cases with unstable plaques and severe calcification without systemic complications. CAS was mainly performed for cases with stable plaques, and cases with a high risk of CEA, even if unstable plaques were present. In symptomatic cases, CAS was performed at least 2 weeks after symptoms. Written informed consent was obtained from all patients. Inclusion criteria were >80% asymptomatic internal carotid artery (ICA) stenosis and >50% symptomatic ICA stenosis. Plaques were diagnosed by MRI and ultrasound. OCT study during CAS was performed for 14 lesions defined as ‘unstable’ on MRI. We did not include patients with creatinine levels >1.2 mg/dL, and lesions with distal ICA elongation. Carotid ultrasound or contrast enhanced CT was performed to examine restenosis and in-stent thrombosis during the follow-up period.

Plaque MRI

Carotid MRI using a 3 T imaging machine (Magnetom Verio; Siemens, Erlangen, Germany)
was performed before the procedure. T1 and T2 weighted images of the carotid artery, including the area with the highest rate of stenosis and plaque, were obtained. T1 weighted image parameters were as follows: repetition time (TR), 500; echo time (TE), 13; and slice thickness, 2.0. T2 weighted image parameters were: TR, 4200; TE, 86; and slice thickness, 3.0 mm. The relative signal intensity (rSI) of plaque components was calculated in relation to the sternocleidomastoid muscle on T1 weighted images and in relation to the submandibular gland on T2 weighted images. On T1 weighted images, rSI >1.5 was defined as ‘high’, meaning unstable. On T2 weighted images, rSI >1.5 was defined as ‘high’.

Ultrasound assessment of plaque
Plaque characters was assessed by ultrasound using the Gray–Weale classification: type 1, predominantly echolucent with a thin echogenic cap; type 2, intermediate echolucent lesions with small areas of echogenicity; type 3, intermediate echogenic lesions with small areas of echolucency (<25%); and type 4, uniformly echogenic lesions.13

CAS procedure
Dual oral antiplatelets beginning at least 5 days before the CAS procedure were administered. Local anesthesia was performed for all patients to allow continuous monitoring of the level of consciousness and motor function. Systemic anticoagulation was achieved by administration of heparin to maintain an activated clotting time of at least 275 s. For 12 lesions, an 8 F or 9 F guiding catheter with a temporary occlusion balloon (Optimo; Tokai Medical Products, Aichi, Japan) was navigated to the external carotid artery (ECA), and a distal filter protection device (FilterWire EZ; Stryker, Fremont, California, USA) was navigated to the common carotid artery (CCA) from the femoral artery, a PurcuSurge Guardwire (Medtronic, Minneapolis, Minnesota, USA) was navigated to the external carotid artery (ECA), and a filter protection device (FilterWire EZ; Stryker, Fremont, California, USA, or Spider FX; Medtronic, Minneapolis, Minnesota, USA) crossed the stenotic lesions with CCA and ECA occlusion. Distal protection was achieved using a flow reversal system and a distal filter. For two lesions with severe atherosclerosis obliterans, a 6 F guiding sheath was navigated to the CCA from the brachial artery and the distal filter protection device crossed the stenotic lesions. Distal protection was achieved only with the use of the distal filter. Pre-dilatation was performed using a 3.5–5.0 mm balloon catheter, if necessary. A carotid Wallstent (Stryker, Fremont, California, USA) was deployed and post-dilatation was performed using a 4.0–7.0 mm balloon catheter. In five cases, the stents were overlapped according to the findings of the OCT analysis.

Diffusion weighted (DW)-MRI was performed within 1–2 days after CAS. Carotid ultrasonography or CT angiography was used to evaluate restenosis of the stented lesions. In the case of unstable plaque, dual oral antiplatelets were continued for at least 3 months, whereas in the case of overlapping stents, dual oral antiplatelets were continued for at least 6 months. Subsequently, dual oral antiplatelet regimens were discontinued when in-stent plaque protrusion or restenosis was not detected on ultrasound examination. Single oral antiplatelet administration was continued.

OCT technique
Carotid OCT images were acquired 2–3 times for each of the 14 lesions: before stent deployment, after dilatation of the stent, and after the overlapping of stents in cases that required it. Dragonfly (St Jude Medical, St Paul, Minnesota, USA), optical fiber used for the investigation of the frequency domain of the OCT system was encapsulated within a rotating torque wire (0.014 inch compatible) used with a rapid exchange 2.6 F catheter compatible with a 6 F guiding catheter to scan a 75 mm artery segment for 2.1 s (pullback speeds up to 36 mm/s). Once the cerebral protection device was deployed in a straight portion of the ICA distal to the stenotic lesion, the calibrated OCT catheter was advanced over the 0.014 inch guide wire of the filter and completely passed over the lesion that needed to be scanned. Pullbacks were started while the CCA and ECA were occluded in cases using balloons mechanically injecting 20 mL of 50% saline diluted contrast medium (Iodixanol 270 mg/mL) to completely replace blood from the artery. Injections were performed through the use of a guiding catheter. Flow arrest within 20 s by occlusion of the CCA and ECA were needed to obtain the OCT data. When a guiding catheter without a temporary occlusion balloon was used, pull-back was started under the same conditions. After stent deployment, the same OCT maneuvers were repeated.

Assessment of OCT images
OCT data were stored using the available OCT systems (Lumenix Optis Imaging System; St Jude Medical) and analyzed by two experienced OCT readers (TM and YH) using dedicated software with an automated contour detection algorithm (Off-line Review Software, V.C.0.2; St Jude Medical). Images were considered non-analyzable if any portion of the cross sectional image was out of the screen, if there was a fold-over artifact, or if intraluminal blood impaired the assessment of a continuous 270 degree arc. The percentage of the stenosis diameter was calculated on the basis of OCT derived North American Symptomatic Carotid Endarterectomy Trial criteria as follows: distal reference lumen diameter—minimal lumen diameter/distal reference lumen diameter×100.11

Definitions of lesion morphology indicating ‘vulnerable’ plaque, such as lipid, thin-cap fibroatheroma (TCFA), plaque disruption, ulceration, calcified, thrombus, or macrophage accumulation, were determined based on previous coronary OCT studies.14 15 TCFA was defined as plaque with lipid content ≥2 quadrants and a fibrous cap with its thinnest part measuring <65 μm.

Cross sectional OCT images within the stented segment of the ICA were evaluated at 1 mm intervals for the presence of tissue prolapse and malapposition. Tissue prolapse was defined as the protrusion of tissue between stent struts extending inside a circular arc connecting the adjacent struts. The distance from the arc to the greatest extent of protrusion was used as a quantitative measure.16 Malapposition was defined when the distance measured from the surface of the blooming (the inner and outer contours of each strut reflection) to the lumen contour was greater than the total thickness of the stent strut plus one-half of the blooming. Regarding carotid stent thickness, a well apposed strut had a protrusion distance ranging from 10 to 200 μm,4 and a malapposed strut had a protrusion distance >200 μm.14 12

Statistical analysis
Continuous variables, such as age and creatinine values, are presented as mean (SD). χ2 analysis and the Fisher exact probability test were performed for categorical variables, such as the rate of tissue prolapse or stent malapposition; p<0.01 was considered significant.
RESULTS
OCT procedures and clinical results
Baseline patient characteristics are shown in table 1. In symptomatic patients, the mean time from the qualifying event to the OCT study was 29 days (range 15–172 days). Successful revascularization with <30% residual stenosis in each case was confirmed by angiography. No technical or neurological complications occurred during OCT pullbacks. High signal on DW-MRI was detected in 21% (3/14 lesions), and all were asymptomatic. Among cases with a high signal on DW-MRI, none had overlapping stents, and OCT analysis showed no tissue prolapse >500 μm. In one case, delayed cerebral infarction occurred 9 months after the procedure (details below). Post-procedural ischemic neurological deficits were not seen within 6 months. Restenosis examined by ultrasound was not detected in any lesion.

OCT results
Plaque characteristics observed before the procedure are shown in table 2. After initial stent placement in 14 lesions, OCT analysis within the stent segment at 1 mm intervals produced a mean of 48±7.9 slices in each lesion; 83% were analyzable. The reasons for non-analyzable frames were out of screen images (15.5%) and the presence of residual blood impairing proper assessment (1.5%). A total of 562 cross sectional OCT images (mean, 40±9.4 slices) were analyzed to assess tissue prolapse and stent apposition. After overlapping stent placement in five lesions, OCT analysis within the stent segment produced a mean of 47±6.0 slices in each patient; 91% were analyzable and 214 cross sectional OCT images (mean 43±7.6 slices) were analyzed. The reasons for non-analyzable frames were out of screen images (8.4%) and the presence of residual blood impairing proper assessment (0.5%). After initial stent placement, slices with tissue prolapse between the stent struts were found in 30%, slices with tissue prolapse >500 μm were found in 7.8%, and slices with at least one malposed strut were found in 56%.

Five of seven lesions had plaque prolapse >500 μm after single stent placement and additional stents were overlapped. A representative case is shown in figure 1. Slices with tissue prolapse between the stent struts was observed in 26% of cases after initial stent placement and in 16% after overlapping stent placement; plaque prolapse significantly decreased with overlapping stents (p=0.008). In particular, slices with tissue prolapse >500 μm were observed in 15% after initial stent placement and in 2.3% after overlapping stent placement; tissue prolapse >500 μm significantly decreased with overlapping stents (p<0.001). Slices with stent apposition of at least one malposed struts were found in 47% and 42% after initial and overlapping stent placement, respectively, with no significant differences (p=0.28).

Case of delayed ischemic embolization
A patient (case No 6 in table 2) experienced sudden left hemiparesis and had right carotid stenosis with unstable plaque diagnosed. CAS was performed 15 days after onset (figure 2A–D). The patient recovered to having slight dysarthria. Carotid ultrasound performed 4 and 7 months after the procedure showed no floating plaque in the stent. Nine months after the procedure, the patient experienced a sudden onset of dysarthria due to right frontal cortical infarction despite continuing dual oral antiplatelets. Ultrasound showed floating plaque in the deployed stent. Emergent CAS was performed for occlusion of the CCA and ECA with a distal filter protection device in the ICA (figure 2E–H). Initial OCT showed abundant embedded plaque; OCT analysis showed slices with any tissue prolapse in 45% and with tissue prolapse >500 μm in 30%. The first overlapped stent decreased any prolapse to 30% and >500 μm prolapse to 16%. The second overlapping stent decreased any prolapse to 10% and >500 μm prolapse to 5%. No ischemic events occurred and the floating thrombus was not detected by ultrasound for 13 months after the second procedure, and the patient had slight dysarthria, indicating a modified Rankin scale score of 1.

DISCUSSION
In this OCT study, CAS with CC stents for unstable plaque resulted in tissue prolapse between the stent struts for all lesions and in 30% during slice evaluations at 1 mm intervals. Plaque prolapse could cause post-procedural embolic complications following CAS; however, the available imaging systems (angiography, IVUS, ultrasound, CT) could not clearly detect plaque prolapse. OCT clearly detected plaque prolapse compared with IVUS. De Donato et al. performed an OCT analysis and reported a 23.3% incidence of plaque prolapse in 1 mm interval slices using CC stents.

For intra-procedural plaque prolapse between stent struts, in-stent balloon angioplasty and overlapping stents have been used to reduce plaque prolapse. In this study, overlapping stents significantly reduced tissue prolapse, in particularly plaque >500 μm, although overlapping stent placement did not increase stent malapposition. This was thought to be due to the low pressure of CC stents. However, overlapping stents could not suppress all plaque protrusions.
<table>
<thead>
<tr>
<th>Case No</th>
<th>Symptoms, stenosis (%)</th>
<th>OCT plaque morphology</th>
<th>Procedure</th>
<th>OCT plaque morphology</th>
<th>Pre/Post (mm)</th>
<th>Outer diameter/length (mm)</th>
<th>Tissue prolapse*</th>
<th>Malapposition*</th>
<th>No of high signal on DW-MRI</th>
<th>Follow-up (months)</th>
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<td>1</td>
<td>Amaurosis fugax, 75</td>
<td>Disruption, ulceration, TCFA, white thrombus, lipid</td>
<td>Balloon dilatation</td>
<td>Stent</td>
<td>4/4</td>
<td>8/29 and 8/21</td>
<td>29 (14/49)</td>
<td>15 (7/47)</td>
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<td>Disruption, lipid</td>
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<td></td>
<td>4/6</td>
<td>10/31 and 10/24</td>
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<td>26 (11/43)</td>
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<td>Disruption, TCFA, lipid</td>
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<td></td>
<td>5/7</td>
<td>10/31 and 10/24</td>
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<td>8 (4/48)</td>
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<td>Disruption, lipid</td>
<td></td>
<td></td>
<td>4/5</td>
<td>8/21 and 8/21</td>
<td>18 (9/49)</td>
<td>11 (5/49)</td>
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<td>8/29 and 6/22</td>
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<td>Disruption, ulceration, lipid, macrophage infiltration</td>
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<td>10/31</td>
<td>16 (8/31)</td>
<td>6 (3/18)</td>
<td>6 (3/18)</td>
<td>Minor stroke (9 months later)</td>
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<td>63 (29/29)</td>
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<td>21 (7/33)</td>
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<td>8/29</td>
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<td></td>
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<td>None/5</td>
<td>8/29</td>
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<td>4.5/4.5</td>
<td>10/31</td>
<td>19 (6/31)</td>
<td>77 (24/31)</td>
<td>0 (0/24)</td>
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</table>

*N* per evaluated slices in parentheses.

DW-MRI, diffusion weighted MRI; OCT, optical coherence tomography; TCFA, thin-cap fibroatheroma.

This OCT study showed that 56% of slices had at least one malapposed struts with CC stents. Stent malapposition after CAS was common, particularly in CC; de Donato et al.\(^\text{10}\) reported in OCT analysis that 34.5% of struts had malapposition after CAS using CC stents, and that there were significantly higher rates of malapposition with CC stents than with open cell stents. Incomplete coronary artery stent strut apposition was related to an increased rate of long term stent thrombosis.\(^\text{19, 20}\) However, delayed stent thrombosis after CAS was thought to be rare even though stent malapposition occurred more frequently with CAS than with coronary stent placement. The discrepancy between carotid and coronary stent malapposition might be due to the stent materials.\(^\text{21}\) Bare metal stents are used for carotid arteries and drug eluting stents are used for coronary arteries. In addition, there are differences between vessel diameters.

In this study, post-procedural DW-MRI showed high signals in 21% of cases. In these lesions, the rate of tissue prolapse after initial stent placement was not significantly different compared with lesions without high signals. Overlapping stents, tissue prolapse between stent struts, and stent malapposition may not be related to microembolism from the lesion within 1–2 days after the procedure.

In this study, the number of embedded and malapposed struts were not evaluated, because near infrared light could not penetrate struts remarkably embedded into the tissue prolapse and because the number of struts could not be counted accurately after overlapping.

OCT for carotid lesions had some limitations. First, OCT studies required a blood free environment, and therefore mechanical injection of half of the concentration of the contrast medium was increased during the procedure. Second, OCT evaluation was difficult in elongated lesions because the OCT system could not reach the elongated ICA distal to the culprit lesion. Third, the penetration depth for OCT was 5–6 mm; therefore, CCA lesions were prone to out of screen artifacts. In this study, 15.5% of OCT slices were excluded from the assessment because of out of screen artifacts, and they were mainly those in the CCA where tissue prolapse is likely to occur less frequently than in the ICA. Therefore, 30% of tissue prolapse on the slice based analysis might be overestimated. Fourth, in OCT...
ischemic stroke

analysis, small plaque prolapse may be confused with a small thrombus: red thrombus is detected as highly backscattering with a high attenuation, and white thrombus is detected as less backscattering, homogeneous, and with low attenuation.15 In this study, almost all of tissue prolapse from the stent struts was considered to be plaque, however, it might be difficult to differentiate between small plaque prolapse and small thrombus.

Study limitations

This was a single center study with a limited number of patients. The selected lesions were biased in unstable plaques and in non-elongated lesions. In addition, no multivariate analysis was performed. Tissue prolapse and stent malapposition after CAS are affected by several factors: some are patient related (age, diabetes, use of statin, etc), some are lesion related (plaque composition, ulceration, etc), some are stent related (design, type, size, etc), and some are procedure related (need for predilatation, post-dilatation, maximum dilatation pressure, etc).

In this study, ‘unstable plaque’ was not a pathological diagnosis. MRI is a well established imaging modality for carotid plaque characterization and T1 WI has a very high sensitivity in detecting unstable plaque that reflects lipid-rich plaque and hemorrhage. However, the rSI values varied because of the difference between 1.5 T and 3 T MRI, and cut-off values for ‘unstable’ were not determined.19 20 In this study, rSI >1.5 of T1 WI obtained with 3.0 T MRI was defined as ‘unstable plaque’ to increase the sensitivity of the assumed unstable plaque.

CONCLUSIONS

OCT during CAS using CC stents for unstable plaque showed many instances of tissue prolapse between stent struts. The placement of overlapping stent significantly reduced tissue prolapse, particularly for those >500 μm. However, CC stents used for unstable carotid plaque may not solve the problem of tissue prolapse between stent struts.

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Contributors

KH was the main operator of the endovascular treatment, designed the research, and drafted the manuscript. SO and MK were the main assistants in patient consent. KH was the main operator of the endovascular treatment, designed specimen pathology. J Cardiovasc Surg (Torino) 1988;29:676–81.


