

Comparison of different carotid stent designs in endovascular therapy of severe carotid artery stenosis

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Abstract

Background: One of the major periprocedural risks of carotid artery stenting is embolism caused either by plaque debris or by local thrombus forming. Double-layer micromesh stent design has shown to lower the chance of debris embolism but might have a slightly higher risk of local thrombus forming. Thus, we compared two different stent designs regarding safety and outcome profile in elective patients with high-grade carotid artery stenosis using a self-expanding, double-layer micromesh carotid stent system (DLCS) or a self-expanding hybrid carotid stent system (HCS). **Methods:** A single-center, open-label, retrospective cohort study of 67 consecutive, elective patients with high-grade symptomatic and asymptomatic carotid stenosis was executed at a comprehensive stroke center. Outcome measures were reocclusion rate, periprocedural symptomatic ischemic events, as well as other periprocedural complications, and recurrent stroke and mortality at 30 days' follow-up. **Results:** Thirty-two patients (24% women, median age 75 years (interquartile range (IQR) 71–80) were treated with DLCS, and 35 patients (29% women, median age 71 years (IQR 63–76) years) with HCS. In both groups, pretreatment carotid stenosis degree was similar (median NASCET of 80%). Successful deployment was achieved in all cases without technical failure, and both groups did not differ in reocclusion rates, recurrent stroke, and mortality within 30 days. **Conclusions:** DLCS and HCS revealed to have similar safety and outcome profile in elective patients with high-grade symptomatic as well as asymptomatic carotid artery stenosis.

Keywords

Double-layer micromesh stent, stent design, hybrid carotid stent system, carotid stenting, carotid artery, atherosclerotic, stroke

Introduction

Atherosclerotic carotid artery stenosis is a relevant cause of ischemic stroke. Nowadays, carotid artery stenting (CAS) is an alternative treatment option to surgical carotid endarterectomy (CEA) in symptomatic as well as asymptomatic carotid artery stenosis, and it appears to be similarly effective as stroke rate between 30 days and several years are comparable.^{1,2} However, in the peri-interventional period, some studies from the past century found a higher risk of stroke with CAS compared to CEA due to the procedural-related risks.³ Most neurological events occurred between day 1 and day 30.⁴ Besides cerebral protection devices—which might prevent from peri-interventional events⁵—several carotid stent systems with different stent designs have been developed, as stent designs might influence the

chance of distal embolic events.⁴ Recently, several carotid stents with a dual micromesh stent design have shown promising safety results.^{6–9} A small study showed that plaque protrusion rate—a potential source of distal emboli—is significantly lower in new-generation double-layer stents compared to conventional carotid stents.¹⁰ Self-expanding nitinol double-layer micromesh carotid stent systems,

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designed to prevent periprocedural embolic events^{9,11} belong to the latest generation of carotid stent systems and have been effective in periprocedural stroke prevention.¹² But there is evidence that DLCS have a higher reocclusion rate in emergent carotid stenting compared to a monolayer stent system.¹³

Thus, we looked at whether different stent designs might have influence on clinical outcome. Therefore, the aim of this study was to compare the stent designs of a DLCS to an HCS regarding safety and outcome profile in elective patients with symptomatic and asymptomatic high-grade carotid stenosis.

Methods

This study was a retrospective, open-label, monocenter cohort study executed at a tertiary stroke center between 2014 and 2018. The study with waived informed consent was approved by the local ethics committee (Ethikkommission Nordwest- und Zentralschweiz EKNZ 2018-01202). Patients were eligible when they were >18 years with either symptomatic or asymptomatic high-grade carotid stenosis ($\geq 70\%$, North American Symptomatic Carotid Endarterectomy Trial (NASCET)) electively (median time from event-to-intervention 5 days (interquartile range (IQR) 3–8 days)) treated with either a DLCS or an HCS.

Patients with tandem stenosis or emergent carotid stenting were excluded.

Study devices

As a representative of a DLCS, we used the CASPER stent system (MicroVention Inc., Tustin, California, USA)—a self-expanding, nitinol-based, double-layer micromesh stent system with closed cell structure and very small stent cell size area of $390\text{--}900\text{ }\mu\text{m}^2$ —was used.^{9,11} As a representative of an HCS, we used the Cristallo Ideale stent system (Medtronic, Minneapolis, Minnesota, USA)—a self-expanding hybrid stent system that consists of closed cell design in the central part and open cell design in the proximal and distal part of the stent combining the advantages of both stent cell designs—open and closed mesh stents—was used.¹⁴ The choice of the carotid stent system was firstly at the discretion of the treating neuro-interventionalist and secondly also depended on the availability of the novel DLCS, which became more frequent over the time. The most commonly used stent type in the DLCS group was the CASPER $7\text{ mm} \times 40\text{ mm}$ ($n = 14$, 44%). The most commonly used HCS stent type was the Cristallo SE $7/10\text{--}40\text{ mm}$ ($n = 30$, 86%). Mostly, a distal protection device was used in both groups (Table 1). The most common distal protection device was Spider FX™ 4 that was used in 48% of all cases, followed by the Spider FX™ 5 type, which was used in 39% of all cases. In three patients, the deployment of a distal protection device failed for local anatomical reasons (HCS group: 2 (6%) vs. DLCS

group 1 (3%), $p = 0.51$). In only a few cases—all in the HCS group ($n = 2$; $p = 0.17$)—where the stent system could not directly advance over the lesion pre-dilatation of the stenosis was necessary. Overall, median deployment time of the DLCS stent system with 17 min (IQR 14–22 min) was for a trend faster compared to the HCS stent system with 20 min (IQR 15–28 min), $p = 0.09$ (Table 1).

Procedure

All procedures were performed under conscious sedation. A biplane angiography system (Allura Xper, Phillips, the Netherlands) was used for the endovascular procedures. All patients received dual antiplatelet therapy (DAPT) with aspirin and clopidogrel prior to intervention. An additional heparin bolus adjusted for body weight, according to activated clotting time blood test, was administered. Retrograde access was obtained from the right common femoral artery. After a diagnostic four-vessel angiogram, the lesion was explored by a microwire (synchro, Stryker Neurovascular, Salt Lake, Utah, USA) under fluoroscopic guidance. Whenever possible, a protection device (Spider FX™ embolic protection device, Medtronic) was delivered in over-the-wire technique. Then, the carotid stent systems were centered over the lesion and the stent deployed. If necessary, additional angioplasty was done. In cases where the stent system could not be directly advanced over the lesion, pre-dilatation was performed.

Patients were kept under DAPT with aspirin and clopidogrel for 3 month post-interventional period. They received a lipid-lowering medication, and cerebrovascular risk factors such as hypertension were controlled and medically treated.

Imaging

Cerebral angiography was used for the exact assessment of the carotid stenosis degree pre- and postprocedural according to the NASCET criteria.¹⁵

Within 24 h after the procedure, all patients were monitored with an ultrasound for immediate restenosis and hyper-perfusion syndrome. Additionally, this post-interventional ultrasound served as baseline measurement for follow-up. After a follow-up of 3 months, patients were again monitored with ultrasound executed by a vascular neurologist. The carotid stenoses were assessed according to the grading criteria proposed by the neurosonology research group of the World Federation of Neurology.¹⁶

Outcome measures

Primary outcome parameters were measured by the rate of periprocedural symptomatic stroke (day 0–30), stent patency at clinical and radiological follow-up within 90 days assessed by a trained vascular neurologist, and the

Table 1. Population, stenosis and technical characteristics.

Population characteristics	DLCS <i>n</i> = 32	HCS <i>n</i> = 35	<i>p</i> Value
Age (years), median (IQR)	75 (71–80)	70 (63–76)	0.07
Sex: male, <i>n</i> (%)	24 (75)	25 (71)	0.74
Hypertension, <i>n</i> (%)	27 (84)	30 (86)	0.88
Dyslipidemia, <i>n</i> (%)	21 (66)	25 (71)	0.61
Diabetes mellitus type II, <i>n</i> (%)	9 (28)	8 (23)	0.62
Obesity, <i>n</i> (%)	6 (19)	8 (23)	0.68
Atrial fibrillation, <i>n</i> (%)	6 (19)	1 (3)	0.035
Kidney disease, <i>n</i> (%)	8 (25)	5 (14)	0.27
Smoker, <i>n</i> (%)	19 (59)	20 (57)	0.85
NIHSS score on admission, median (IQR)	0 (0–1)	1 (0–4)	0.08
Clinically asymptomatic stenosis, <i>n</i> (%)	5 (16)	4 (11)	0.62
TIA, <i>n</i> (%)	11 (34)	9 (26)	0.44
Stenosis characteristics			
Left side, <i>n</i> (%)	20 (63)	21 (60)	0.84
Preprocedural stenosis degree NASCET, median (IQR)	80 (70–90)	80% (70–90)	0.46
Contralateral side			
History of CEA, <i>n</i> (%)	3 (9.4)	2 (6)	
Occlusion of contralateral CCA/ICA, <i>n</i> (%)	3 (9.4)	1 (2.9)	
Stenosis degree NASCET ≥ 50 –99%, <i>n</i> (%)	5 (16)	5 (14)	
Technical characteristics			
Conscious sedation, <i>n</i> (%)	32 (100)	35 (100)	0.07
Distal protection Device, <i>n</i> (%)	27 (87)	34 (97)	
Pre-dilatation, <i>n</i> (%)	0 (0)	2 (5.71)	0.17
Post-dilatation, <i>n</i> (%)	27 (84)	28 (80)	0.12
Stent deployment time (min), median (IQR)	17 (14–22)	22 (15–28)	0.09
Stent types in use, <i>n</i> (%)			
CASPER 7 × 30 mm	14 (44)		
CASPER 8 × 30 mm	10 (31)		
CASPER 8 × 40 mm	8 (25)		
Cristallo SE 6/9–30 mm		4 (13)	
Cristallo SE 6/9–40 mm		1 (3)	
Cristallo SE 7/10–40mm		30 (86)	

CEA: carotid endarterectomy; DLCS: double-layer carotid micromesh stent; HCS: hybrid stent system; IQR: interquartile range; NASCET: North American Symptomatic Carotid Endarterectomy Trial; NIHSS score: National Institute of Health Stroke Scale Score; TIA: transient ischemic attack; CCA: common carotid artery; ICA: internal carotid artery.

rate of periprocedural complications (dissections, vessel perforation, any kind of bleeding, and deployment failure) as well as technical success rate defined as proper stent deployment with residual stenosis degree $<30\%$. Furthermore, we looked at mortality rate and favorable clinical outcome—defined as modified Ranking Scale score ≤ 2 within 90 days.

Statistics

Statistical analysis was done with STATA 14.2 (StataCorp, College Station, Texas, USA). Group comparison for non-parametric data was done using Wilcoxon rank-sum test and for continuous data with two-sided *t*-test. The value of $p < 0.05$ was considered as statistically significant.

Results

The two groups revealed similar mean ages ($p = 0.07$) and did not differ in female:male ratio with 1:3 each (Table 1).

Except for atrial fibrillation with a higher frequency in the DLCS group (19%; $n = 6$) compared to the HCS group (3%; $n = 1$) ($p = 0.035$), there was no difference regarding vascular risk factors (Table 1). Hypertension was the most common vascular risk factor (Table 1). A third of the patients presented with transient ischemic event (Table 1). Overall, the median NIHSS score was low in both groups (Table 1). There was an equal median preprocedural stenosis degree according to the NASCET criteria of 80% in both groups ($p = 0.46$). In both groups, the lesion was most commonly found on the left side (Table 1).

There were slightly—but insignificantly—more periprocedural complications as well as peri-interventional clinical symptomatic ischemic events occurred in the HCS group compared to the DLCS group, respectively (Table 2). Probably due to the small sample size, these results are not significant. There were no clinical symptomatic ischemic events in the DLCS group. In both groups, no dissections, vessel perforation, peri-interventional intracranial hemorrhages, or significant stent deployment failure occurred.

Table 2. Summary of outcome measures.

Outcome measures	DLCS <i>n</i> = 32	HCS <i>n</i> = 35	<i>p</i> Value
Symptomatic ischemic events, <i>n</i> (%)	0 (0)	2 (5.71)	0.17
Reocclusion rate within 30 days, <i>n</i> (%)	1 (3)	1 (2.9)	0.95
Follow-up mRS score, median (IQR)	0 (0–1)	0 (0–2)	0.92
Death rate within follow-up, <i>n</i> (%)	1 (3)	1 (2.9)	0.95
In-hospital mortality, <i>n</i> (%)	0 (0)	1 (2.9)	0.39
Restenosis rate, <i>n</i> (%)	2 (6.25)	2 (5.71)	0.92
Periprocedural complications, <i>n</i> (%) ^a	1 (3.12)	4 (11.3)	0.19
Postprocedural stenosis degree NASCET (%), median (IQR)	10 (0–20)	10 (0–25)	0.52
Technical success rate, <i>n</i> (%) ^b	29 (90)	27 (77)	0.13

DLCS: double-layer micromesh carotid stent; HCS: hybrid stent system; IQR: interquartile range; NASCET: North American Symptomatic Carotid Endarterectomy Trial; mRS: modified Ranking Scale.

^aPeriprocedural complications are defined as dissection, vessel perforation, any kind of bleeding and deployment failure.

^bTechnical success rate is defined as proper stent deployment with residual stenosis degree <30%

Postprocedural stenosis degree was good in both groups with median residual stenosis degree of 10% (IQR 0–20) in the DLCS group and 10% (0–25) in the HCS group (Table 2) with an insignificantly higher technical success rate in the DLCS group. One reocclusion has to be reported for each group. Both reocclusions occurred within 30 days due to poor drug compliance of the DAPT. At follow-up, both groups did not differ regarding stent patency with patent stent system.

In each group, one patient died during the follow-up period. In the HCS group, a patient died because of severe pneumonia and consecutive complications during the hospital stay. In the DLCS group, one patient died due to a fatal intracranial bleeding caused by a hyper-perfusion syndrome and poor drug compliance in terms of antihypertensive agents 17 days postprocedure.

In both groups, the median clinical follow-up outcome was excellent with mRS of 0 (IQR 0–1) and the median mRS of 0 (IQR 0–2) in the DLCS group and HCS group, respectively (0.92) (Table 2).

Discussion

Our cohort study demonstrated that DLCS revealed a similar safety and outcome profile compared to the latest HCS in elective patients with high-grade artery stenosis.

Meanwhile, it is evident that both CAS and CEA are effective in protecting patients from stroke in the long run.^{1,2} However, there is a higher propensity of stroke in CAS patients—especially in the peri-interventional period—compared to CEA patients. In subgroup analyses of the ICSS trial and a recent meta-analysis including 20

CAS/CEA studies demonstrated that in 40.3% of the CAS patients presented with post-interventional diffusion-weighted magnet resonance imaging lesions compared to CEA patients with only 12.2%.^{17,18} These results were partially explained by the mesh type design. This is supported by a subgroup analysis of the SPACE trial, which demonstrated more ipsilateral strokes in open cell stents compared to close cell stents (11 vs. 5.5%).¹⁹ Novel stent designs were introduced to solve this issue. Thus, an optimal stent should cover the whole plaque lesion and additionally the stent struts should protect the vessel lumen from plaque disruption, which might be a source of ischemic embolic events.²² There are several stent systems on the market that offer a DLCS such as the CGuard (InspireMD, Boston, Maryland, USA), the Roadsaver (Terumo, Tokyo, Japan), and the CASPER stent system. The CGuard stent system as well the Roadsaver stent system showed good results in small mono-arm studies with low incidence of periprocedural ischemic events with 23% to 37.7% ischemic events compared to monolayer stent studies with up to 60%.^{7,8} Additionally, a recent mono-arm cohort study using CASPER stent with a distal protection device showed lower asymptomatic stroke rates compared to historic controls.¹² So far all of the DLCS mono-arm studies reported no symptomatic ischemic events.^{9,20} We could support this finding with no symptomatic stroke compared to two symptomatic strokes in the self-expanding hybrid stent system group ($p = 0.17$). Our relatively low rate of ischemic events is explained by the fact that we did not perform post-interventional magnetic resonance (MR) control as long as patients were not clinically symptomatic. It remains a matter of debate whether subclinical ischemic events are of importance, since the clinical outcome is favorable, despite the relatively high incidence of asymptomatic events detected on MR.²¹

Contrary to a study reporting higher rate of stent occlusion in emergent carotid stenting using DLCS stent system compared to a single-layer stent system,¹³ we found a similarly low rate of stent occlusion in both the DLCS and HCS, respectively. This observation in our elective cohort may be due to the peri-interventional use of DAPT, which might be a more sufficient protection against the potentially more thrombogenic surface of DLCS than an emergent loading dose of single antiplatelet therapy in emergent carotid stenting. The only two reocclusions of the carotid stent system (in each group one) were caused by poor drug compliance. Thus, it is of utmost importance to adhere patients on DAPT during 90 days after carotid stent implantation.

Our postprocedural residual stenoses were similar to those reported by other dual-layer stent studies.¹¹ Furthermore, we had no deployment failure, and no other complications such as dissections or vessel perforations.

Our study has limitations to merit: first, we had no MR follow-up, which might be helpful to detect silent brain infarction. However, it remains a matter of debate whether subclinical ischemic events are of importance. Second,

because of the retrospective nature of this study there was no randomization.

Conclusion

Both carotid stent systems—the self-expanding, double-layer micromesh stent system and the self-expanding hybrid stent system—demonstrated to have a similar safety and outcome profile in elective patients with high-grade carotid artery stenosis.


Declaration of conflicting interests

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