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E-POSTER

Highly-calcific carotid lesions endovascular management in symptomatic and increased-stroke-risk asymptomatic patients using the CGuard™ dual-layer carotid stent system: Analysis from the PARADIGM study

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Background

- Highly calcific carotid stenosis (HCCS) is considered a classic contraindication to endovascular management due to (1) risk of carotid artery perforation/rupture, (2) suboptimal procedural results with conventional carotid stents.
- CGuard™ embolic prevention stent system (CGuard EPS, InspireMD) is a dual-layer carotid stent that is characterized by a remarkably open-cell structure of the nitinol frame and a high radial force; the MicroNet mesh with ultra-closed "micro-cell" structure is positioned outside of the nitinol frame.
- DW-MRI and clinical evidence indicates that CGuard EPS is effective in minimizing peri-procedural and preventing post-procedural cerebral embolization.
- All-comer PARADIGM study evaluates feasibility, safety, and outcome of CAS using routinely the CGuard EPS in consecutive, unselected patients with symptomatic or increased-stroke risk asymptomatic carotid stenosis across all lesion subsets.
- PARADIGM Study has no exclusion criteria other than lack of NeuroVascular Team agreement on revascularization indication and preferred endovascular route

Objectives

To assess feasibility, safety, angiographic, and clinical outcome of highly-calcific carotid stenosis (HCCS) endovascular management using CGuard™ dual-layer carotid stents.

Materials and Methods

- The PARADIGM study (101 patients, 106 lesions) is prospectively assessing routine CGuard use in all-comer carotid revascularization patients
- The focus of the present analysis is HCCS versus non-HCCS lesions. Angiographic HCCS (core laboratory evaluation) required calcific segment length to lesion length ≥2/3, minimal calcification thickness ≥3 mm, circularity (≥3 quadrants), and calcification severity grade ≥3 (carotid calcification severity scoring system [CCSS]; G0-G4) (see Table 1A and 1B).
- Study group clinical characteristics are given in Table 2.
- Precise HCCS characteristics are presented in Table 3.

Table 1A. Highly calcific carotid stenosis (HCCS) angiographic criteria (all four needed for HCCS).

Calcific segment length to lesion length ratio ≥ 2/3
Calcification circularity index ≥ 3*
Calcification thickness ≥3.0 mm
Calcification severity grade ≥3†

* 1 if 1 quadrant, 2 if 2 quadrants, 3 if 3 quadrants, 4 if 4 quadrants † according to Carotid Calcification Severity Scoring (CCSS); five-grade scale of G0 – G4 (Table 2B)

Table 1B. Carotid Calcification Severity Scoring (CCSS); Grade 0-4, best fit evaluation.

Lesion calcification severity		Calcification visibility on still frame	Calcification visibility on cine	Calcification intensity and pattern
G0	No significant calcification	not visible	not visible	• no intensities exceeding that of background present at lesion site
G1	Mild calcification	not visible	barely visible	• poor intensity, • no specific pattern can be determined
G2	Moderate calcification	barely visible	evident	• higher than background intensities • no evident conglomerate present • calcification spots with no eccentric/concentric pattern evident
G3	Severe calcification	evident	evident	• moderate density conglomerate(s) or calcification spots of high density • calcification dominates the lesion • eccentric or concentric pattern
G4	Very severe calcification	evident	evident	• calcification dominates the lesion • massive, compact calcific conglomerate of very high density • concentric pattern inclusive of massive exophytic ("mushroom-like") endoluminal calcification

LESIONS CONSIDERED HCCS HAVE TO (I) FULFILL ANGIOGRAPHIC CRITERIA (TABLE 1A) (II) BE SCORED AT LEAST CCSS G3 (TABLE 1B).

Table 2. Study group characteristics: HCCS lesion vs. non-HCCS lesion patients.

		HCCS patients (n=16)	Non- HCCS patients (n=85)	p- value
Age, median (Q1-Q3), years		75 (68-79)	69 (63-75)	0.005
Male, % (n)		43.7 % (7)	75.3% (64)	0.011
Symptomatic, % (n)		37.5% (6)	60 % (51)	0.096
Index lesion (CAS):	LICA, % (n)	31.2 % (5)	54.1 % (46)	0.093
	RICA, % (n)	68.8 % (11)	45.9 % (39)	0.093
	LICA+RICA, % (n)	12.5 % (2)	5.9 % (5)	0.339
CAD, % (n)		75 % (12)	61.2 % (52)	0.292
h/o MI, % (n)		25 % (4)	30.6 % (26)	0.654
h/o CABG or PCI, % (n)		43.7 % (7)	36.5 % (31)	0.581
AFib, % (n)		12.5% (2)	8.2 % (7)	0.583
Diabetes, % (n)		43.7 % (7)	41.2 % (35)	0.848

CAD - coronary artery disease; MI - myocardial infarction; CABG - coronary artery bypass grafting; AFib - atrial fibrillation

Table 3. HCCS characteristics. Data are given as median (Q1-Q3) or proportion (n).

HCCS baseline characteristics	
Calcification severity, Grade 3 % (n)	68.8 (11)
Grade 4 % (n)	31.2 (5)
Calcification circularity index 3/4 % (n)	6.2 (1)
4/4 % (n)	93.8 (15)
Minimal calcification thickness, mm	4.99 (4.06-5.72)
Calcification length, mm	17.66 (13.97-21.44)
Calcification length /lesion length ratio,	0.82 (0.76-0.93)
Calcification intensity (CI; mean grey value; AU)	190 (158.5-218.5)
Calcification volume, mm^3	619 (441-911)
HCCS post-procedural characteristics	
Minimal calcification thickness, mm	2.88 (2.44-3.50)
Calcification thickness change, mm	1.94 (1.46-2.40)

Results

- In PARADIGM study population (101 patients, 51–86 years, 54.4% symptomatic, 106 lesions) 16 lesions were classified as HCCS according to study criteria
- CCSS evaluation was reproducible, with weighted kappa (95% CI) of 0.73 (0.58–0.88) and 0.83 (0.71–0.94) for inter- and intra-observer reproducibility respectively (see Fig 1).
- HCCS postdilatation pressures were higher than those in non-HCCS; 22 (20–24) versus 20 (18–24) atm, p=0.028; median (Q1–Q3). Angiography-optimized HCCS-CAS was feasible and free of contrast extravasation or clinical complications (see Table 4).
- Overall residual diameter stenosis was single-digit but it was higher in HCCS; 9 (4–17) versus 3 (1–7) %, p=0.002. At 30 days and 12 months HCCS in-stent velocities were normal and there were no adverse clinical events.

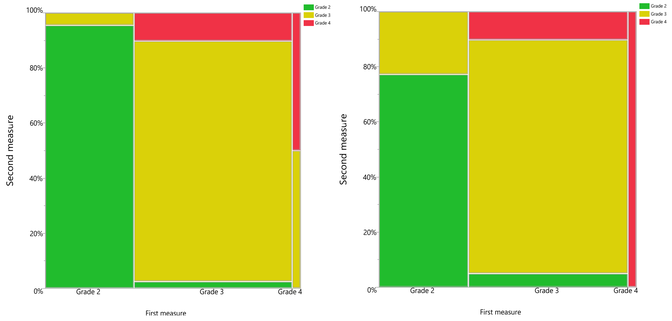

Fig 1. Agreement charts (left – intra-observer; right – inter-observer) for calcification severity evaluation according to CCSS in lesions of at least moderate severity by any of the two analysts. For lesions classified as severely calcified by the fist analyst 5% were classified as moderate and 10% as very severe by the second analyst. In case of very severe calcifications both analyst gave the same results in 100%. In general 83% of lesions were classified identically by both analysts. Weighted kappa (95% CI) was 0.73 (0.58–0.88) and 0.83 (0.71–0.94) for inter- and intra-observer reproducibility, respectively.

Table 4. Lesion characteristics and management (HCCS vs. non-HCCS)

	HCCS (n =16)	non - HCCS (n= 90)	p- value
Before CAS			
PSV, median (Q1-Q3), m/s	3.6 (2.8-4.6)	3.65 (2.6-4.5)	0.951
EDV, median (Q1-Q3), m/s	0.96 (0.8-1.32)	1.1 (0.78- 1.63)	0.382
Diameter stenosis, median (Q1-Q3), %	81.0 (73.0-92.5)	86 (75-91)	0.556
CAS			
Proximal EPD type, % (n)	43.8 (7)	46.7 (42)	0.830
Distal EPD type, % (n)	56.2 (9)	53.3 (48)	0.830
Non-compliant balloon pre-dilation, % (n)	31.2 (5)	2.2 (2)	0.002
Non-compliant (NC) balloon post-dilatation, % (n)	43.8 (7)	1.1 (1)	<0.001
Maximal post dilatation pressure, median (Q1-Q3), mmHg	22 (20-24)	20 (18-24)	0.028
After CAS			
Residual diameter stenosis, median (Q1-Q3), %	10.3% (4-42)*	3.0% (1-7)	0.003
In-stent PSV, median (Q1-Q3), m/s	0.87 (0.61-1.24)	0.58 (0.46-0.75)	0.001
In-stent EDV, median (Q1-Q3), m/s	0.19 (0.13-0.29)	0.15 (0.12-0.20)	0.080

* immediate result; note that in one case stent optimization was staged due to a severe bradycardia-asystole that occurred with mild post-dilatation attempt (on a separate occasion optimization was performed under temporary pacing; stent diameter 9.0x30 mm, maximal balloon diameter 6.0x20 mm, maximal pressure 24atm, leading to a residual stenosis of 17% rather than the initial 46%, and the group median value of 10.3%, p<0.001 vs. non-HCCS); PSV - peak systolic velocity; EDV- end diastolic velocity; EPD - embolic protection device

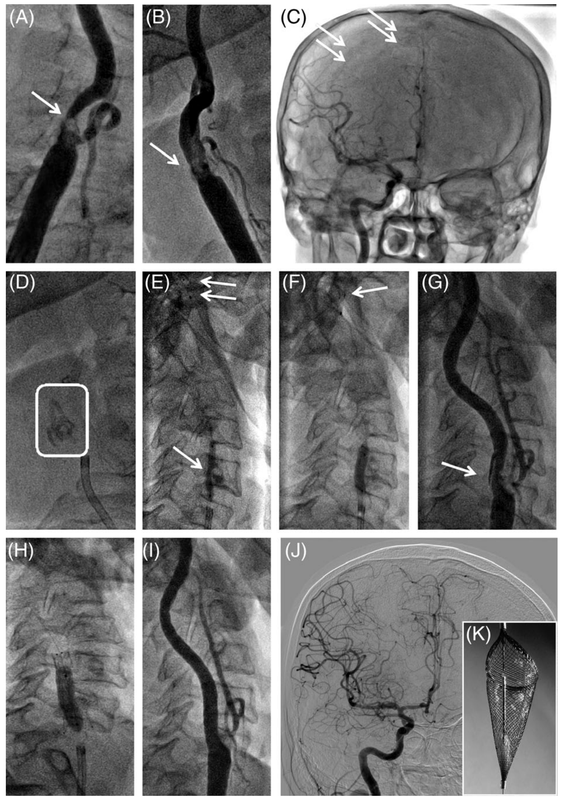

Fig 2. Angiographic examples of HCCS-CAS using the CGuard™ EPS. Elective CAS procedure in 69 years old, neurologically asymptomatic female patient, with progressive right internal carotid artery (RICA) stenosis in the context of positive family history of stroke, with severe heart failure (Fallot heart surgery in the childhood). (A, B, D) A tight highlycalcified lesion in proximal RICA, (arrows, box), associated with impaired supply to the right hemispheric vessels ([C] double arrows, compare with [J]). A channel for wire crossing was barely visible (A), the lesion involved the external carotid artery (ECA) ostium (A, B). Distal NPD was used (Spider Fx 7.0 filter arrows in [E]). (E) Shows predilatation with a semicompliant balloon 3.0 × 20 mm, followed by a 4.5 × 20 mm coronary noncompliant balloon (F). Adequate vessel preparation led to a dissection in absence of contrast extravasation (G). An 9.0 × 30 mm CGuard EPS stent implantation was followed by postdilatation (5.5 × 20 mm semicompliant balloon at 24 atm) (H) (angiogram, note patent ECA) and (I) shows final result of this procedure, with no residual stenosis. (J) Shows an optimal right hemisphere supply achieved with the procedure (with now some "overshooting" to the left side). The Spider filter filled with debris is in (K). The procedure was clinically uneventful and the patient remained neurologically asymptomatic at follow-up.

Conclusion

- CGuard HCCS endovascular management was feasible and safe.
- A novel algorithm to grade carotid artery calcification severity was reproducible and applicable in clinical study setting.
- Larger HCCS series and longer-term follow-up are warranted.