JACC: CARDIOVASCULAR INTERVENTIONS VOL. 14, NO. 17, 2021

PERIPHERAL

1-Year Results From a Prospective Experience on CAS Using the CGuard Stent System

The IRONGUARD 2 Study

Pasqualino Sirignano, MD,[a] Eugenio Stabile, MD, PhD,[b] Wassim Mansour, MD, PhD,[a] Laura Capoccia, MD, PhD,[a] Federico Faccenna, MD,[a] Francesco Intrieri, MD,[c] Michelangelo Ferri, MD,[d] Salvatore Saccà, MD,[e] Massimo Sponza, MD,[f] Paolo Mortola, MD,[g] Sonia Ronchey, MD,[h] Barbara Praquin, MD,[h] Placido Grillo, MD,[i] Roberto Chiappa, MD,[j] Sergio Losa, MD,[k] Francesco Setacci, MD,[k] Stefano Pirrelli, MD,[l] Maurizio Taurino, MD,[m] Maria Antonella Ruffino, MD,[n] Marco Udini, MD,[o] Domenico Palombo, MD,[p] Arnaldo Ippoliti, MD,[q] Nunzio Montelione, MD, PhD,[r] Carlo Setacci, MD,[s] Gianmarco de Donato, MD,[s] Massimo Ruggeri, MD,[t] Francesco Speziale, MD[a]

ABSTRACT

OBJECTIVES The aim of this study was to evaluate the 1-year safety and efficacy of a dual-layered stent (DLS) for carotid artery stenting (CAS) in a multicenter registry.

BACKGROUND DLS have been proved to be safe and efficient during short-term follow-up. Recent data have raised the concern that the benefit of CAS performed with using a DLS may be hampered by a higher restenosis rate at 1 year.

METHODS From January 2017 to June 2019, a physician-initiated, prospective, multispecialty registry enrolled 733 consecutive patients undergoing CAS using the CGuard embolic prevention system at 20 centers. The primary endpoint was the occurrence of death and stroke at 1 year. Secondary endpoints were 1-year rates of transient ischemic attack, acute myocardial infarction, internal carotid artery (ICA) restenosis, in-stent thrombosis, and external carotid artery occlusion.

RESULTS At 1 year, follow-up was available in 726 patients (99.04%). Beyond 30 days postprocedure, 1 minor stroke (0.13%), four transient ischemic attacks (0.55%), 2 fatal acute myocardial infarctions (0.27%), and 6 noncardiac deaths (1.10%) occurred. On duplex ultrasound examination, ICA restenosis was found in 6 patients (0.82%): 2 total occlusions and 4 in-stent restenoses. No predictors of target ICA restenosis and/or occlusion could be detected, and dual-antiplatelet therapy duration (90 days vs 30 days) was not found to be related to major adverse cardiovascular event or restenosis occurrence.

CONCLUSIONS This real-world registry suggests that DLS use in clinical practice is safe and associated with minimal occurrence of adverse neurologic events up to 12-month follow-up. (J Am Coll Cardiol Intv 2021;14:1917–1923)

From the [a]Vascular and Endovascular Surgery Unit, Department of Surgery, "Sapienza" University of Rome, Rome, Italy; [b]Division of Cardiology, Department of Advanced Biomedical Sciences, University Federico II, Naples, Italy; [c]Unit of Vascular and Endovascular Surgery, Annunziata Hospital, Cosenza, Italy; [d]Vascular and Endovascular Surgery Unit, Mauriziano Umberto I Hospital, Turin, Italy; [e]Division of Cardiology, Mirano Public Hospital, Mirano, Italy; [f]Division of Vascular and Interventional Radiology, Udine University Hospital, Udine, Italy; [g]Department of Vascular and Endovascular Surgery, Galliera Hospital, Genoa, Italy; [h]Unit of Vascular Surgery, Surgical Specialty Department, S. Filippo Neri Hospital, Rome, Italy; [i]Division of Cardiology, Sant. Anna Hospital, Catanzaro, Italy; [j]Department of Vascular and Endovascular Surgery, Sandro Pertini Hospital, Rome, Italy; [k]Cardiovascular Department, MultiMedica IRCCS Scientific Institute, Milan, Italy; [l]Division of Vascular Surgery, Carlo Poma Hospital, Mantova, Italy; [m]Unit of Vascular Surgery, Department of Clinical and Molecular Medicine, "Sapienza" University of Rome, Sant'Andrea Hospital, Rome, Italy; [n]Department of Diagnostic Imaging and Radiotherapy - Vascular Radiology, Città della Salute e della Scienza di Torino, Turin, Italy; [o]Vascular Surgery, Moriggia Pelascini Hospital, Gravedona, Como, Italy; [p]Vascular and Endovascular Surgery Unit, IRCCS Ospedale Policlinico San Martino, University of Genoa, Genoa, Italy; [q]Vascular Surgery Unit, Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy; [r]Vascular Surgery, University of Campus Biomedico of Rome, Rome, Italy; [s]Department of Medicine, Surgery and Neuroscience, Vascular and Endovascular Surgery, University of Siena, Siena, Italy; and [t]Vascular Surgery, San Camillo de Lellis Hopital, Rieti, Italy.

ISSN 1936-8798 https://doi.org/10.1016/j.jcin.2021.05.045

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

CAS = carotid artery stenting

DAPT = dual-antiplatelet therapy

DLS = dual-layered stent(s)

ECA = external carotid artery

EPD = Embolic Protection Device

ICA = internal carotid artery

MACE = major adverse cardiovascular event(s)

NIHSS = National Institutes of Health Stroke Scale

TIA = transient ischemic attack

Carotid artery stenting (CAS) has emerged as a valid alternative to carotid endarterectomy in both symptomatic and asymptomatic patients requiring extracranial internal carotid artery (ICA) revascularization (1).

However, plaque protrusion through the stent struts seems to be related to periprocedural ipsilateral strokes, negatively affecting clinical outcomes of CAS with conventional stents because of the risk for cerebral embolization causing ipsilateral periprocedural new strokes. Dual-layered stents (DLS) (2-4), a new generation of devices, were recently developed to overcome this adverse procedural occurrence, consisting of Nitinol stents combined with a mesh (Nitinol or polyethylene terephthalate) that potentially captures plaque debris and thrombus between the stent and the arterial wall (5).

Several small studies (6-9) and a patient-based meta-analysis (10) have reported more than satisfactory safety and clinical efficacy at 30 days. At 12-month follow-up, a wide range of restenosis rates emerged among different DLS-based studies and different DLS devices (11).

The aim of this study was to assess the clinical efficacy of the CGuard DLS (Inspire MD) with respect to death, stroke, and in-stent restenosis at 12-month follow-up from a real-world, large prospective Italian study.

SEE PAGE 1924

METHODS

STUDY DESIGN. From January 2017 to June 2019, 20 Italian centers prospectively enrolled patients undergoing CAS using a specific DLS, the CGuard embolic prevention system (12). The present study conformed to the Declaration of Helsinki, and ethics committees were notified. All patients enrolled in the study gave written informed consent to undergo CAS and be included in the study. For each patient, data were anonymized and collected in a dedicated web-based database.

STUDY POPULATION. Inclusion criteria considered the degree of stenosis and related symptoms: symptomatic stenosis of the ICA ≥50%, asymptomatic stenosis ≥80%, and life expectancy >5 years. Exclusion criteria were target ICA reference diameter smaller than 3 mm or larger than 9 mm, history of previous life-threatening contrast media reaction, contraindications to aspirin and clopidogrel, known allergy to nickel or titanium, uncorrectable bleeding disorders, evidence or previous (<12 months) intracranial hemorrhage or brain surgery, history of intracerebral aneurysms or arteriovenous malformation, common carotid artery ostial lesions (unless untreated simultaneously with index CAS), occlusion of target vessels, intraluminal thrombosis, previously stented target carotid artery, and inability to comply with enrollment and follow-up requirements.

All CAS procedures considered in the present analysis were performed according to each operating unit's therapeutic standard and devices' specific instructions for use (12).

CONCOMITANT THERAPY. All patients received dual-antiplatelet therapy (DAPT) at a standard dose for at least 2 days before the CAS procedure (alternatively, intraprocedural 600-mg clopidogrel loading was performed). For intraprocedural anticoagulation, unfractionated heparin (70-100 IU/kg) was administered to maintain an activated clotting time >250 seconds. After the procedure, DAPT, including aspirin and clopidogrel, was continued for at least 1 month. After the first month postprocedure, clopidogrel was discontinued according to each enrolling institution's clinical protocol, while aspirin was continued indefinitely.

PATIENT FOLLOW-UP. Following hospital discharge, participants were clinically assessed at 30 days and 12 months per protocol; unplanned visits were also recorded, if available. At each visit, carotid duplex ultrasound, neurologic assessment, physical examination, and adverse event recording were routinely conducted.

ENDPOINTS. The primary endpoint was the occurrence of death and stroke at 1 year; secondary endpoints were 1-year rates of transient ischemic attack (TIA), acute myocardial infarction (AMI), restenosis, in-stent thrombosis, and external carotid artery (ECA) occlusion.

Major adverse cardiovascular events (MACE) were defined as death, stroke, and AMI.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 1, 2021; revised manuscript received May 10, 2021, accepted May 18, 2021.

At each institution, a neurologist or a National Institutes of Health Stroke Scale (NIHSS)-certified physician evaluated all patients during hospitalization and following an event that occurred during follow-up.

Neurologic complications were classified as follows: 1) TIA was defined as a new transient episode of neurologic dysfunction caused by focal brain or retinal ischemia without imaging evidence of acute infarction; 2) minor stroke was defined as a new neurologic deficit that entirely resolved in 30 days or increased the NIHSS score by ≤3 points compared with the preprocedural evaluation; and 3) major stroke was defined as a new neurologic deficit that persisted for >30 days and increased the NIHSS score by ≥4 points compared with the preprocedural evaluation.

Restenosis was defined as either the detection of stenosis of 50% to 99% or occlusion on ultrasonographic examination performed after stenting, with the degree of stenosis determined according to the norms of the local ultrasonography laboratory (12). Patients with restenosis between 70% and 99% underwent new endovascular procedures.

STATISTICAL ANALYSIS. Data on demographic characteristics, preprocedural computed tomographic angiographic evaluation, and intraprocedural details were entered into a prospectively compiled web-based database and further analyzed as potential risk factors for postprocedural outcomes. Continuous variables are expressed as mean ± SD and were compared using paired or unpaired Student's *t*-tests. Categorical variables are expressed as counts and percentages and were compared using the Fisher exact test or the chi-square test. Odds ratios and risk ratios to study the primary endpoint were calculated for clinical and procedural variables. A 2-sided *P* value of <0.05 was considered to indicate statistical significance. Long-term outcomes were determined using Kaplan-Meier curves and log-rank tests. All analyses were performed using SPSS version 23.0 (IBM).

RESULTS

Demographic and procedural characteristics of the study population have been previously published (12). Demographic, anatomical, and procedural characteristics of enrolled patients are reported in **Table 1**.

As previously reported, up to 30 days from discharge, 4 strokes (1 fatal and 3 minor) and 1 death were recorded. Intraprocedural ECA occlusion occurred in 8 patients (1.09%) (12).

DAPT was maintained in all patients till the 30th postoperative day per protocol and till the 90th day in 295 patients (40.63%) according to each institution's clinical practice.

One-year data were available for 726 out the 733 initially treated patients, for a rate of loss to follow-up of 0.95%.

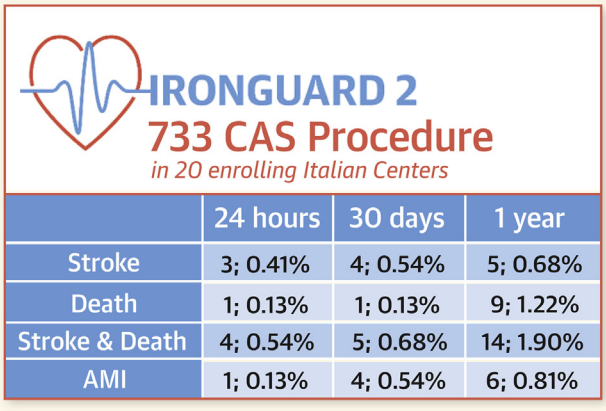
From day 31 to day 365, the rate of any ipsilateral stroke was 0.13%, while new cerebral adverse events

TABLE 1 Demographic, Anatomical, and Procedural Characteristics of Patients Included in the Registry

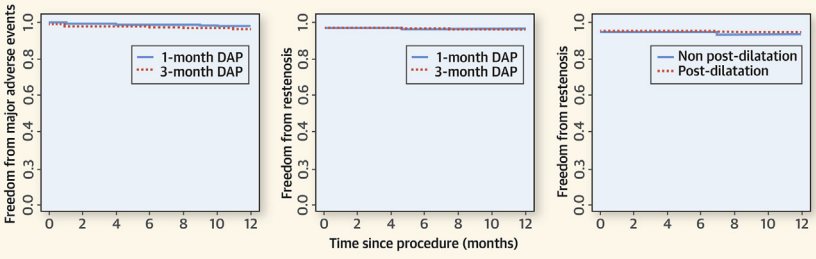
Age, y	73.03 ± 7.84 (39-97)
Male	516 (70.39)
Octogenarians	141 (19.23)
High risk	386 (52.66)
Symptomatic stenosis	131 (17.87)
Hypertension	622 (84.85)
Diabetes	264 (36.01)
Dyslipidemia	552 (75.30)
Smoking history	429 (58.52)
CAD history	278 (37.92)
Right-side internal carotid artery	395 (53.81)
Plaque	
Hyperechoic	163 (22.23)
Isoechoic	107 (14.59)
Hypoanechoic	181 (24.69)
Dishomogenous	172 (23.46)
Ulcerated	40 (5.45)
Thin fibrous cap	29 (3.99)
Post-CEA restenosis	41 (5.59)
Aortic arch	
Type I	369 (50.34)
Type II	268 (36.56)
Type III	39 (5.32)
Bovine	57 (7.78)
Tortuosity	
None	194 (26.46)
Low	289 (39.42)
Moderate	191 (26.05)
Severe	59 (8.07)
Severe calcification	199 (27.14)
Severe thrombosis	147 (20.05)
Femoral access	713 (97.27)
Any protection system	731 (99.72)
Proximal protection	138 (18.82)
Predilatation	169 (23.05)
Postdilatation	607 (82.81)

Values are mean ± SD (range) or n (%).
CAD = coronary artery disease; CEA = carotid endarterectomy.

CENTRAL ILLUSTRATION **Event Rates in the IRONGUARD 2 Study**



	24 hours	30 days	1 year
Stroke	3; 0.41%	4; 0.54%	5; 0.68%
Death	1; 0.13%	1; 0.13%	9; 1.22%
Stroke & Death	4; 0.54%	5; 0.68%	14; 1.90%
AMI	1; 0.13%	4; 0.54%	6; 0.81%



		Incidence without the variable N (%)	Incidence with the variable N (%)	*P* (OR; 95% CI)
Hypertension		0 (0)	5 (0.80)	0.34 (NA)
Diabetes		2 (0.42)	3 (1.13)	0.26 (2.68; 0.44-16.16)
Dyslipidaemia		1 (0.55)	4 (0.72)	0.80 (1.31; 0.14-11.83)
Smoking history		3 (0.98)	2 (0.46)	0.41 (0.48; 0.08-2.91)
Coronary artery disease		3 (0.65)	2 (0.71)	0.92 (1.09; 0.18-6.57)
Octogenarians		3 (0.51)	2 (1.41)	0.23 (2.82; 0.46-17.06)
High clinical risk		2 (0.59)	2 (0.50)	0.49 (0.53; 0.08-3.25)
Symptomatic stenosis		3 (0.49)	2 (1.52)	0.19 (3.09; 0.51-18.71)
Plaque	Hyperechoic	4 (0.70)	1 (0.61)	1.00 (NA)
	Isoechoic	3 (0.47)	2 (1.89)	
	Hypo-anechoic	4 (0.72)	1 (0.55)	
	Disomogeneous	5 (0.89)	0 (0)	
	Ulcerated	4 (0.57)	1 (2.5)	
	Thin fibrous cap	5 (0.71)	0 (0)	
	Post-CEA restenosis	5 (0.72)	0 (0)	
	Unstable	4 (0.60)	1 (1.44)	0.41 (2.42; 0.26-22.01)
Aortic arch	Type I	2 (0.54)	3 (0.81)	1.00 (NA)
	Type II	3 (0.64)	2 (0.74)	
	Type III	5 (0.72)	0 (0)	
	Bovine	5 (0.73)	0 (0)	
Tortuosity	None	4 (0.74)	1 (0.51)	1.00 (NA)
	Low	2 (0.45)	3 (1.03)	
	Moderate	4 (0.73)	1 (0.52)	
	Severe	5 (0.74)	0 (0)	
	Significant	4 (0.82)	1 (0.40)	0.50 (0.48; 0.05-4.32)
Severe calcification		3 (0.56)	2 (1.00)	0.51 (1.79; 0.29-10.83)
Severe thrombosis		3 (0.51)	1 (0.68)	0.99 (0.99; 0.11-8.98)
Distal protection		1 (0.71)	4 (0.67)	0.76 (0.70; 0.07-6.84)
Predilatation		4 (0.70)	1 (0.59)	0.80 (0.83; 0.09-7.50)
Postdilatation		1 (0.80)	4 (0.65)	0.86 (1.20; 013-10.88)

Sirignano, P. et al. J Am Coll Cardiol Intv. 2021;14(17):1917–1923.

Continued on the next page

were registered in 5 patients: 1 minor stroke and 4 TIAs (0.55%).

Cumulatively, 8 patients (1.10%) died between postoperative days 31 and 365: 4 malignancies (0.55%), 1 suicide (0.13%), 1 undefined complication of Guillain-Barré syndrome (0.13%), and 2 fatal AMIs (0.27%).

Consequently, the 365-day cumulative stroke rate was 0.68%; immediate (24 hours), 30-day, and 1-year rates of stroke, death, stroke and death, and AMI are depicted in the **Central Illustration**.

On duplex ultrasound examination, ICA restenosis was found in 6 patients (0.82%): 2 occlusions left untreated because of unknown time of onset, and 4 asymptomatic in-stent restenoses (2 of which, evaluated as >70% and presenting peak systolic velocity >450 cm/s, were successfully treated by CAS). New computed tomographic angiography was performed only in those patients requiring reintervention. No additional ECA was found to be occluded during follow-up, thus the ECA patency rate at 1 year was 98.8% (718 of 726).

On univariate analysis, none of the clinical, anatomical, or procedural characteristics were found to be statistically related to new stroke occurrence during the entire study period (**Central Illustration**).

On log-rank analysis, DAPT duration was not found to be related to MACE ($P = 0.17$) (**Central Illustration**) or restenosis occurrence ($P = 0.62$) (**Central Illustration**); furthermore, rate of freedom from restenosis was not affected by the intraoperative performance of stent postdilatation ($P = 0.97$) (**Central Illustration**).

DISCUSSION

This study demonstrates that: 1) in a real-world evaluation of CAS, DLS were safely used for guideline-based treatment of symptomatic or asymptomatic extracranial carotid artery stenosis, with low rates of MACE and restenosis at 12 months; 2) prolongation of DAPT beyond 30 days (up to 90 days) postprocedure does not seem to reduce MACE or restenosis rate; and 3) intraprocedural postdilation does not affect restenosis rate at 1 year.

IRONGUARD 2 represents, to date, the largest prospective multicenter multispecialty registry on the use of mesh-covered stents. More than 700 consecutive CAS patients were enrolled during the study period, treated using the CGuard DLS, and followed for 12 months. All centers have established experience with the new stent system, as previously reported in detail (12).

Although it is well known that the majority of cerebral adverse events after CAS occur in the first 30 postprocedural days, it cannot be denied that risk still exists beyond the first month. Data from previously published studies on different DLS (6-9) showed a low but significant risk for new stroke occurrence between postoperative days 30 and 365. A patient-level showed 6 minor strokes (1.08%) during hospitalization, 1 ipsilateral stroke between hospital discharge and 30 days, and 4 additional strokes (0.71%) by the end of 1-year follow-up (11). The present experience, reporting results on patients treated with only a single DLS implantation, showed even better performance during the 1-year period: 3 strokes (1 fatal [0.41%]) were registered at hospital discharge, 1 at 1 month, and an additional stroke at 12 months, the latter 2 strokes both minor. Overall, the meta-analysis accounted for 10 strokes (1.79%) during the entire 12-month observation period (11), while our multicenter experience cumulatively registered 5 strokes (0.68%), confirming the more than satisfactory results achievable in an unselected patient population. However, these satisfactory results are related to a series of nonrandomized patients, mostly treated for severe asymptomatic stenosis; this could partially justify the good rate of adverse neurologic events reported.

None of the clinical, anatomical, or technical preoperative or intraoperative characteristics analyzed were statistically associated with stroke occurrence during the entire study period; this

CENTRAL ILLUSTRATION Continued

(Top left) 24-hour, 30-day, and 1-year rates of stroke, death, stroke and death, and acute myocardial infarction. **(Bottom left)** Kaplan-Meier estimates of freedom from major adverse events in patients who received 30- or 90-day dual-antiplatelet therapy (DAPT), freedom from restenosis in patients who received 30- or 90-day DAPT, and freedom from restenosis in patients submitted or not to intraprocedural postdilatation **(Right)** Clinical, anatomical, and procedural characteristics potentially affecting stroke occurrence during the entire study period. CEA = carotid endarterectomy; DAP = dual-antiplatelet therapy; NA = not available.

finding is particularly important because the use of this device minimizes the risk related to the treatment of symptomatic patients. Although these results seem encouraging, they should be interpreted with caution given the relatively small percentage of symptomatic patients in the study (131 of 733 [7.87%]), even if compared with data reported from other similar studies (6-9).

Despite the widespread adoption of CAS procedures, the duration of postoperative DAPT after DLS implantation (11) is still unclear. As suggested by the available guidelines, every patient who undergoes CAS, regardless the type of implanted stent, should receive DAPT throughout the 30-day perioperative period. After that, no additional benefit of DAPT over antiplatelet monotherapy is reported. However, those recommendations were based largely on the coronary research because of the lack of data from large trials in CAS patients, especially with the new-generation DLS (13). In particular, no data on a comparison between DAPT and antiplatelet monotherapy, beyond the 30-day perioperative period, have ever been reported.

Recently, reported datasets have specifically investigated the possible correlation existing between DLS implantation, DAPT, and stent thrombosis, demonstrating a significantly lower rate of thrombosis in subjects who underwent prolonged (3-month) DAPT (14,15). However, those data were derived from experiences performed in emergently treated patients, mostly using DLS other from the CGuard embolic prevention system. Indeed, in this study, no stent thrombosis occurred during the first postoperative month, and only 2 occlusive restenoses were detected at 12-month follow-up. When dividing the patient population into 2 groups according to DAPT duration (30 or 90 days), no difference in freedom from cardiovascular adverse events at 1 year could be detected. This finding is in contrast to the conclusion of a recent meta-analysis (16) and does not support the need to prolong DAPT beyond 30 days after CAS with a DLS. Such data should be considered hypothesis generating for future investigational studies.

In this registry, DLS use was associated with a low rate (<1%) of restenosis, and the lack postdilatation was not associated with a higher occurrence of restenosis during follow-up. In consideration of this observation, stent postdilatation should not be considered a mandatory part of a CAS procedure using this new-generation device.

STUDY LIMITATIONS. The main limitation was in the design of the study, a prospective registry, which was not randomized and did not allow us to compare the results with a control patient population.

Moreover, per study protocol, no centralized core laboratory analysis of ultrasound images was performed, and degree of stenosis was determined by the standards of the local ultrasonography laboratory. Although all evaluations were performed by highly skilled operators, potential interpretation bias in defining the exact restenosis degree could not be absolutely excluded.

Clopidogrel response was not assessed in enrolled patients. Consequently, no data on this specific issue are available for patients experiencing adverse new neurologic events or in-stent occlusion or restenosis.

Randomized studies are needed to confirm the early- and long-term durability of the CAS procedure using DLS.

CONCLUSIONS

The 1-year results of the IRONGUARD 2 study suggest that the use of DLS could make it possible to achieve low rates of MACE and restenosis, regardless of patients' clinical and anatomical features or the procedural techniques adopted. Undeniably, our data should be validated in a randomized trial, prospectively evaluating results with a proper control population.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Pasqualino Sirignano, Vascular and Endovascular Surgery Division, Department of Surgery "Paride Stefanini," "Sapienza" University of Rome, Policlinico Umberto I, Viale del Policlinico 155, 00161 Rome, Italy. E-mail: pasqualino.sirignano@uniroma1.it.

PERSPECTIVES

WHAT IS KNOWN? The need for increased plaque coverage to decrease the risk for debris dislodgement through stent struts has led to the design of DLS, which are able to trap and exclude thrombus and/or plaque debris to prevent embolic events from the target lesion. The safety and clinical efficacy of these devices have been proved up to 30 days. More recent studies have demonstrated that these devices are also associated with good clinical outcomes at 1-year follow-up, with a quite variable restenosis rate among the studies.

WHAT IS NEW? DLS could represent a solution in preventing events related to embolization through stent struts. The IRONGUARD 2 study represents the largest real-world study on patients undergoing CAS with DLS. The use of DLS has proved safe and effective in lowering periprocedural and postprocedural neurologic complications. Thirty-day and 12-month follow-up results confirm their role in effectively preventing brain embolic events. The restenosis rate with this particular type of stent is very low, with only 2 patients requiring reintervention.

WHAT IS NEXT? These data can be considered hypothesis generating toward the design of a large-scale clinical trial to definitively investigate the long-term safety and efficiency of this endovascular technique of carotid revascularization.

REFERENCES

1. Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med*. 2016;374:1011–1020.

2. de Donato G, Setacci F, Sirignano P, Galzerano G, Cappelli A, Setacci C. Optical coherence tomography after carotid stenting: rate of stent malapposition, plaque prolapse and fibrous cap rupture according to stent design. *Eur J Vasc Endovasc Surg*. 2013;45:579–587.

3. Bosiers M, Deloose K, Callaert J, et al. Impact of stent design on outcomes of carotid stent angioplasty. *Semin Vasc Surg*. 2018;31:4–8.

4. Capoccia L, Sirignano P, Mansour W, et al. Periprocedural brain lesions prevention in CAS (3PCAS): randomized trial comparing CGuard™ stent vs. Wallstent™. *Int J Cardiol*. 2019;279:148–153.

5. Stabile E, Tesorio T, Esposito G. The modern approach to endovascular carotid revascularisation. *EuroIntervention*. 2016;12:e538–e540.

6. Capoccia L, Sirignano P, Mansour W, Sbarigia E, Speziale F. Twelve-month results of the Italian registry on protected CAS with the mesh-covered CGuard stent: the IRON-Guard study. *EuroIntervention*. 2018;14:1150–1152.

7. Musialek P, Mazurek A, Trystula M, et al. Novel PARADIGM in carotid revascularisation: prospective evaluation of all-comer percutaneous carotid revascularisation in symptomatic and increased-risk asymptomatic carotid artery stenosis using CGuard MicroNet-covered embolic prevention stent system. *EuroIntervention*. 2016;12:e658–e670.

8. Nerla R, Micari A, Castriota F, et al. Carotid artery stenting with a new-generation double-mesh stent in three high-volume Italian centres: 12-month follow-up results. *EuroIntervention*. 2018;14:1147–1149.

9. Bosiers M, Deloose K, Torsello G, et al. Evaluation of a new dual-layer micromesh stent system for the carotid artery: 12-month results from the CLEARROAD study. *EuroIntervention*. 2018;14:1144–1146.

10. Stabile E, de Donato G, Musialek P, et al. Use of dual-layered stents in endovascular treatment of extracranial stenosis of the internal carotid artery: results of a patient-based meta-analysis of 4 clinical studies. *J Am Coll Cardiol Intv*. 2018;11(23):2405–2411.

11. Stabile E, de Donato G, Musialek P, et al. Use of dual-layered stents for carotid artery angioplasty: 1-year results of a patient-based meta-analysis. *J Am Coll Cardiol Intv*. 2020;13(14):1709–1715.

12. Sirignano P, Stabile E, Mansour W, et al. 1-Month results from a prospective experience on CAS using CGuard stent system: the IRONGUARD 2 study. *J Am Coll Cardiol Intv*. 2020;13(18):2170–2177.

13. Naylor AR, Ricco JB, de Borst GJ, et al. Editor's choice—management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg*. 2018;55(1):3–81.

14. de Vries EE, Vonken EJ, Kappelle LJ, Toorop RJ, de Borst GJ. Short-term double layer mesh stent patency for emergent or elective carotid artery stenting. *Stroke*. 2019;50(7):1898–1901.

15. Lamanna A, Maingard J, Kok HK, et al. Carotid artery stenting in acute stroke using a microporous stent device: a single-center experience. *World Neurosurg*. 2019;127:e1003–e1012.

16. Barkat M, Hajibandeh S, Hajibandeh S, Torella F, Antoniou GA. Systematic review and meta-analysis of dual versus single antiplatelet therapy in carotid interventions. *Eur J Vasc Endovasc Surg*. 2017;53(1):53–67.

KEY WORDS carotid artery disease, carotid artery stenting, stroke