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Peri-procedural brain lesions prevention in CAS (3PCAS): Randomized trial comparing CGuard™ stent vs. Wallstent™☆

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ABSTRACT

Background: Aim of this study was to evaluate peri-procedural incidence of new diffusion-weighted-magnetic-resonance-imaging (DWMRI) brain lesions in CAS patients treated by carotid mesh stent (CGuard™) or closed-cell stent (Wallstent™).
Methods: Consecutive patients with asymptomatic carotid stenosis ≥ 70% were submitted to preoperative DW-MRI scan, to exclude the presence of preoperative silent cerebral lesions. Patients were randomized to CGuard or Wallstent. DWMRI was performed immediately after the intervention and at 72-hour postoperatively. Moreover, pre and postoperative Mini-Mental-State-Examination Test (MMSE) and a Montreal-Cognitive-Assessment (MoCA) test were conducted, and S100β and NSE neurobiomarkers were measured at 5-time points (preoperatively, 2, 12, 24, and 48 h postoperatively).
Results: From January 2015 to October 2016, sixty-one consecutive eligible patients were submitted to preoperative DWMRI scan. Three patients were excluded because of preoperative silent cerebral lesions. In 29 CGuard patients, 1 developed a minor stroke and 8 silent new lesions were observed in the 72 h-DWMRI (31%): 4 lesions were ipsilateral, and 4 lesions were contra or bilateral. In 29 Wallstent patients, 7 clinically-silent new lesions were found in the 72 h-DWMRI (24.1%; $p = 0.38$). In 4 cases lesions were ipsilateral and in 3 cases contra or bilateral. S100B values doubled at 48 h in 24 patients, and among them 12 presented new DWMRI lesions. 48-h S100B increase was significantly related to 72-h DWMRI lesions ($p = 0.012$).
Conclusions: In our experience both stents showed an acceptable rate of subclinical neurological events with no significant differences at 72-hour DWMRI between groups. Bilateral/contralateral lesions suggest that periprocedural neurological damage may have extra-carotid sources.

1. Introduction

1.1. Background

Stroke is one of the most frequent causes of death and morbidity worldwide. Atherosclerotic stenosis of the extracranial internal carotid artery has been invoked as a common causative factor for stroke in over 20% of patients [1]. Although medical therapy can help to prevent the onset and progression of carotid arteriosclerosis, open surgical carotid endarterectomy (CEA) has been the gold standard for treating severe blockage. Alternatively, carotid stent angioplasty (CAS) has been shown to protect patients from future stroke with long-term efficacy similar to CEA [2]. In this context, carotid artery stenting has been shown to be associated with a reduction in the risk of myocardial infarction in high-risk surgical subgroups [2–4]. Nevertheless, it has been considered that the main CAS limitation vs CEA is the relatively superior incidence on clinical stroke [2] (most frequently minor). To study this phenomenon, diffusion-weighted-magnetic-resonance-imaging (DW-MRI) in asymptomatic patients after CAS has demonstrated the incidence of more new cerebral lesions in CAS than in CEA [3]. Likewise, some studies have reported increased level of specific neurobiomarkers following carotid revascularization procedures, in accordance to possible brain embolic events [5,6]. New and improved procedural Embolic Protection Systems (including filters, proximal protection flow-reversal and Trans Carotid Artery Revascularization (TCAR)) has demonstrated neuroprotection in CAS peri-procedural

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events [7,8]. In addition to the peri-procedural period, during the post-procedural period a significant portion of the neurologic events may occur (between 1 and 30 days following the stent implantation). This observation suggests mechanisms such as plaque embolization through the stent struts may occur [8]. In the symptomatic population late complication rates are highest for the open cell types and increase with larger free cell area [9], but despite the increasing use of closed-cell design stents the risk of plaque prolapse through the stent struts and of post-procedural embolism still exists [10]. In order to prevent plaque prolapse, a new stent design has been conceived: CGuard combines the traditional open-cell stent design to an exterior polyethylene terephthalate (PET) mesh that is able to capture and keep in place plaque debris as small as 150–180 μm. CGuard™ has demonstrated post-procedural neuro protection, by reducing new lesions incidence and volume at 1-month FU DWMRI (post-procedural) [11].

The first published prospective studies on the use of CGuard™ stent, the CARENET [11] (Carotid Embolic Protection Using MicroNet) Trial and the PARADIGM [12] Study have shown 0% MACNE (Major Adverse Cardiac or Neurologic Events) at 30-days. The routine per-protocol diffusion-weighted magnetic resonance cerebral imaging (DW-MRI) demonstrated post-procedural embolic prevention efficacy. The CARENET DW-MRI showed a low incidence of any ipsilateral new lesion (s) (37%) after CAS and a very low average lesion volume ($\approx$0.04 cm^3) [11], suggesting >50% reduction in incidence and >10-fold reduction in mean lesion volume when compared to conventional carotid stents [13,14]. Routine thirty-day DW-MRI imaging in CARENET revealed only one small new lesion (0.08 cm^3) and showed complete resolution of all but one peri-procedural lesion [11].

So, if CGuard is protective post-procedurally, never has been previously analyzed the hypothesis that CGuard may be preventive during the peri-procedural period, from the cerebral filters removal up to 3 days postprocedurally, when the carotid plaque may be considered most destabilized by the stent struts apposition and more prone to embolize. Some studies have demonstrated that specific neurobiomarkers are released into circulating blood whenever a brain insult occur [5,6]. Some of them can be detected within few minutes from the neurological ischemic event [15–19] so that their variation in time can help monitoring different phases of a single brain ischemia or multiple occurrences of infracentimetric ischemic insults, as it can sometimes occur during or after carotid revascularization. Moreover, cognitive performance variations can sometimes be observed after multiple microembolic ischemic brain insults [20]. The aim of the present study is to determine the peri-procedural incidence of new DWMRI brain lesions, neuropsychometric tests conversion and neurobiomarkers appraisal, comparing a carotid mesh stent (CGuard™) versus a control group treated with a carotid closed cell stent (Wallstent™). Primary outcome was new DW-MRI lesions in the two randomized stent groups. Secondary end-points were the variation in neuropsychometric test (NPT) scores, and appraisal of neurobiomarkers.

2. Methods

2.1. Trial design

Single-center, randomized controlled trial comparing results between two different carotid stents in patients affected by asymptomatic ≥ 70% carotid artery stenosis and submitted to CAS in accordance with the ICCS-SPREAD Joint Committee consensus [21]. The present study has been registered on ClinicalTrials.gov (NCT02665585).

2.2. Participants

CAS inclusion criteria were: age > 55 years, presence of a carotid stenosis ≥ 70% (NASCET [22] evaluation criteria), with no previous neurologic symptoms referred in the medical history, absence of a previous brain ischemic lesion detected at diffusion-weighted-magnetic-resonance-imaging (DW-MRI). Patients with symptomatic carotid lesions, previous ischemic lesions detected at DW-MRI, or inability to give consent were excluded from the study.

Exclusion criteria for CAS were: significant contraindications to angiography, history of bleeding disorder, or intracranial aneurysm or vascular malformation or hemorrhage, presence of intraluminal thrombus, poor entry points at the femoral artery, type 2–3 arch, bovine arch, severe aortic arch or ipsilateral ostial common carotid or brachiocephalic atherosclerosis, severe proximal common or distal internal carotid artery tortuosity, sharply angulated internal carotid artery, carotid string sign, circumferential calcification of carotid plaque, length of the target lesion requiring more than one stent at contrast-enhanced CT scans.

Eligibility criteria for randomization were: obtained informed consent, compliance to the study protocol. Patients were randomized to receive either carotid Wallstent (Boston Scientific, Marlborough, MA, USA) or C-Guard carotid stent (Inspire-MD, Boston, MA, USA) a new mesh-covered open-cell stent. Written informed consent was obtained before enrollment. The study protocol and informed consent form were approved by the Institutional Ethical Committee.

2.3. Setting

All procedures were performed at the same center with an adequate annual volume experience of the operators [23,24]. Data were collected and analyzed at our Vascular Unit Academic Centre.

2.4. Interventions

Dual antiplatelet therapy was started at least three days before intervention and maintained for at least 1 month post-procedurally. Single antiplatelet therapy was maintained indefinitely. CAS intervention was performed under local anesthesia with a distal embolic protection device in all cases (Filterwire, Boston Scientific, Marlborough, MA, USA). Wallstent or CGuard stent were alternatively used to cover the whole plaque surface. No predilatation was used in the present series.

2.5. Diffusion-weighted magnetic resonance imaging (DWMRI) performance

All patients were submitted to preoperative, immediate postoperative (from 30 min to 1-hour), and 72 h DW-MRI. A comparison between immediate postoperative and 72-hour examinations was performed in order to detect any off-table events. Presence of recent ischemic lesions at preoperative examination was considered an exclusion criterion for entering the study.

2.6. Mini-Mental State Examination (MMSE) test and Montreal Cognitive Assessment (MoCA) test administration and interpretation

All patients were submitted to preoperative and 72-hour postoperative MMSE and MoCA tests in order to prove the effect of CAS-related microemboli on cognitive performance. The research assistant responsible for performing the tests preoperatively and postoperatively in all patients was trained to administer and score the tests. Downgrading in the postoperative examination, such as from normal to some cognitive impairment (1 step), or a difference ≥ 4 in the postoperative score compared with the preoperative value, was considered significant. No psychotropic or sedative medications were administered to the patients before performing tests.

2.7. Neuron-Specific Enolase - NSE and S100β serum levels detection and analysis

The S100 test measures the β-subunit of protein S100 as defined by three monoclonal antibodies with a detection limit of 0.02 μg/L. NSE measurement is based on monoclonal antibodies that bind to the γ-subunit of the enzyme with a minimal measurable concentration of 0.3 μg/L. S100β and NSE proteins were analyzed by the use of automated immunoluminometric assays (S100 Elecsys test, Roche Diagnostics GmbH, Mannheim, Germany; ELSA-NSE, CIS Bio International, Gif-sur-Yvette Cedex, France). Venous blood samples were obtained for each patient preoperatively (basal sample), and at 2, 12, 24, and 48 h after the end of the procedure. Samples were allowed to clot. After centrifugation (1800*g* for 6 min) ≤20 min from collection, serum was stored at −80 °C for later analysis.

2.8. Objective

To demonstrate a decrease in off-table microembolic event rate in patients submitted to CAS with CGuard stent implantation compared to patients with Wallstent implantation, detected by DW-MRI, markers of brain injury, and neuropsychometric tests.

2.9. Outcome measures

Primary outcome measures considered for comparative analysis in the two CAS groups were perioperative off-table (up to 72 h postoperatively) neurological ischemic events clinically (TIA, stroke, permanent focal retinal artery occlusion, neurological death) or subclinically detected (by new DW-MRI lesions).

Secondary outcomes measures were perioperative (up to 72 h postoperatively) ≥0.02 μg/L increase in S100β and/or ≥0.3 μg/L increase in NSE serum levels, ≥5 variation in postprocedural MMSE test score or MoCA test score compared to the preoperative one in the two treatment groups, rate of perioperative local complications (inguinal haematoma, pseudoaneurysm formation, access vessel dissection or thrombosis) or systemic complications (acute myocardial infarction (AMI) detected by myocardial specific enzymes increase and electrocardiographic alterations, transient or permanent renal impairment defined as a creatinine serum level increase ≥ 25% of the basal value, ≥24 h hypotension or bradycardia, respectively defined as systolic blood pressure ≤ 120 mm Hg, and heart rate ≤ 60 bpm, acute respiratory failure requiring prolonged orotracheal intubation).

2.10. Statistical analysis

2.10.1. Sample size estimation

Data from previously published study demonstrated an extremely variable incidence of DWMRI-detected brain microembolism [25]. Based on our experience [5], we considered an incidence of around 40% in patients submitted to CAS with Wallstent implantation. No data are available on 72-hours brain embolism in patients submitted to CGuard implantation, so we speculated a subclinical incidence of neurological events of 10%. We considered a new event any ischemic lesion detected by DWMRI, independently from number or size of lesions recorded. Assuming a type I error $\alpha = 0.05$, a type II error $\beta = 0.20$, so a power $(1\text{-}\beta) = 0.80$, an event rate in the control (Wallstent) group of 0.40 (40%) [5], an event rate in the treatment (CGuard) group of 0.10 (10%), so assuming a 30% event rate reduction in the treatment group, 29 patients were randomly allocated in each treatment group.

2.10.2. Randomization

A computer-generated random allocation sequence was used. A blocked randomization was performed with an allocation ratio 1:1. Allocation concealment was used. Blind postprocedural DW-MRI interpretation, neurobiomarkers levels evaluation, and MMSE and MOCA administration was done by those assessing outcomes.

2.10.3. Results analysis

Categorical variables are reported as numbers and percentages and compared by Fisher and chi-square tests. Continuous data are reported as median and standard deviation and compared by *s*-Student test and ANOVA for multiple samples. Analysis of variance has been used to test the differences among and between groups at different time-points. Moreover, neurobiomarker values have been categorized as follows and analyzed as categorical variables: in every patient variations of S100B and NSE have been analyzed comparing every value with the basal one and the 48-hour value with the basal one, so that every patient has been classified twice as belonging to "increased", "stable", or "decreased" category if a ≥25% variation was detected. NPTs scores were analyzed as continuous values and also categorized and analyzed if a ≥4 increase or decrease between two consecutive assessments was detected.

3. Results

From January 2015 to October 2016 fifty-eight patients were randomized at our Academic Center. Three patients were excluded from the study before randomization because of the presence of preoperative DWMRI clinically silent lesions (Fig. 1). Technical success was 100%. Postdilatation was used in 86.2% of patients. Baseline and procedural features are reported in Tables 1 and 2.

Table 1
Baseline features in 29 CGuard patients and 29 Wallstent patients.

	CGuard	Wallstent	P (OR; 95%CI)
Age (mean ± SD; 95%CI)	70.4 ± 5.91 (66.86–73.94)	68.8 ± 7.43 (65.12–72.45)	0.52
Male sex (n;%)	20 (68.9%)	22 (75.8%)	0.55 (0.70; 0.22–2.25)
Right side (n;%)	19 (65.5%)	12 (41.4%)	0.06 (2.69; 0.92–7.8)
Smoke (n;%)	14 (48.3%)	19 (65.5%)	0.18 (0.49; 0.17–1.41)
Hypertension (n;%)	27 (93.1%)	26 (89.6%)	0.62 (1.55; 0.24–10.09)
Dyslipidemia (n;%)	26 (89.6%)	28 (96.5%)	0.30 (0.31; 0.03–3.16)
Diabetes (n;%)	11 (37.9%)	5 (17.2%)	0.07 (2.83; 0.86–9.94)

In 29 CGuard patients 1 minor stroke (ipsilateral lesion) and 8 clinically silent 72 h-DWMRI lesions detections were recorded (31%), and in 29 Wallstent patients 7 clinically silent 72 h-DWMRI lesions detections were found (24.1%; no statistically significant difference between the two treatment groups; p = 0.38; Table 3).

Two patients presented with immediate postoperative DWMRI lesions. Interestingly, those lesions were no longer detectable at 72 h DWMRI control. According to the site of DWMRI lesions, in 8 CGuard patients 4 had ipsilateral, and 4 contra or bilateral lesions. In 7 Wallstent patients 4 had ipsilateral and 3 contra or bilateral lesions. Mean DWMRI lesion diameter was 3.87 ± 1.53 mm (95%CI 3.307–4.436) in CGuard group and 3.56 ± 1.07 mm (95%CI 2.871–4.253) in Wallstent group (p = 0.49; Table 3). Five or more DWMRI lesions were detected in 5 CGuard patients and in 3 Wallstent patients (p = 0.5). No significant association was encountered with stent postdilatation in patients presenting postoperative DWMRI lesions (p = 0.46).

Within group analysis of neuropsychometric tests (NPTs) showed a significantly better postoperative MoCA score in Wallstent patients

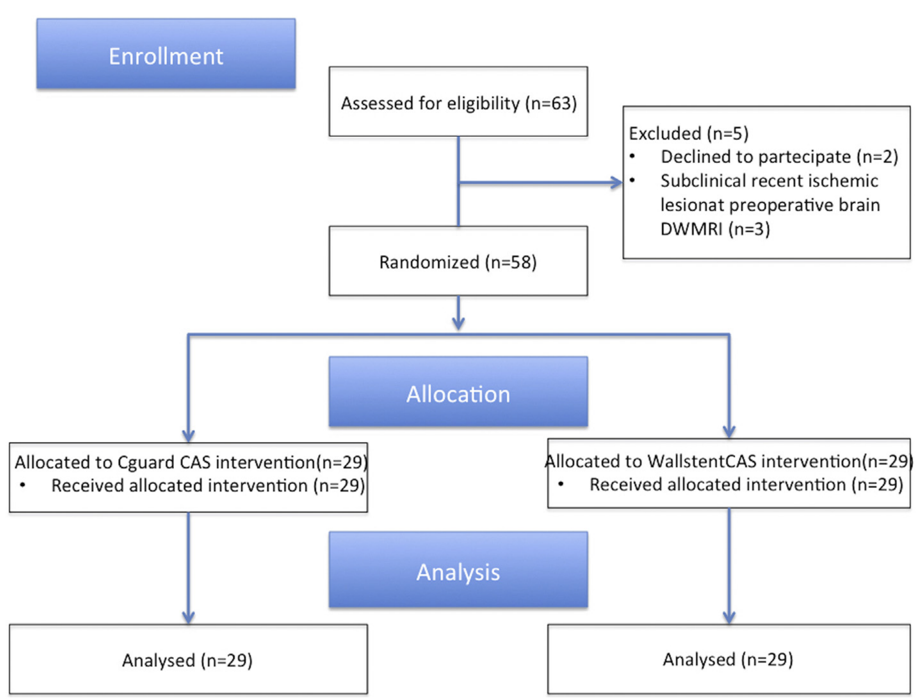

Fig. 1. Peri-procedural brain lesions prevention In CAS (3PCAS) randomized controlled trial randomization flow diagram.

Table 2
Carotid lesion and procedure features in 29 CGuard patients and 29 Wallstent patients.

	CGuard	Wallstent	P (OR; 95%CI)
Stenosis percentage (mean ± SD; 95%CI)	78.7 ± 7.19 (74.81–82.53)	78.9 ± 7.38 (74.93–82.92)	0.92
Femoral access (n;%)	29 (100%)	29 (100%)	1
Distal embolic protection device (n;%)	29 (100%)	29 (100%)	1
Predilatation (n;%)	11 (37.9%)	5 (17.2%)	0.07 (2.93; 0.86–9.94)
Postdilatation (n;%)	22 (75.8%)	19 (65.5%)	0.38 (1.65; 0.52–5.19)
Procedural time (minutes; mean ± SD; 95%CI)	23.7 ± 2.53 (21.89–25.45)	25.6 ± 4.07 (23.73–27.41)	0.14

with respect to preoperative evaluation ($p = 0.03$; Table 3), while analysis of postoperative scores in both groups showed not significant better scores in Wallstent patients ($p = 0.12$ and $p = 0.45$ for MMSE and MoCA, respectively; Table 3). NPTs postoperative scores showed a significant association with the presence of >5 DWMRI lesions, irrespective of lesion site ($p = 0.007$ and $p = 0.03$ for MMSE and MoCA, respectively; Fig. 2).

Neurobiomarker values and variations were not significantly different between the two treatment groups at continuous and categorical analysis (Table 3).

Table 3
Outcomes in 29 CGuard patients and 29 Wallstent patients.

	CGuard	Wallstent	P (OR; 95%CI)
Positive 72 h-DWMRI (n;%)	9 (31%)	7 (24.1%)	0.55 (1.41; 0.44–4.50)
72 h-DWMRI lesion number per pt (mean ± SD; 95%CI)	3.56 ± 2.30 (2.05–5.06)	3.43 ± 1.81 (1.72–5.13)	0.91
72 h-DWMRI lesion diameter (mean ± SD; 95%CI)	3.87 ± 1.53 (3.3–4.43)	3.56 ± 1.07 (2.87–4.25)	0.49
Preprocedural MMSE (mean ± SD; 95%CI)	27.9 ± 3.23 (26.16–29.56)	27.9 ± 2.96 (26.16–29.56)	1
Postprocedural MMSE (mean ± SD; 95%CI)	26.8 ± 2.42 (25.66–27.96)	27.3 ± 1.7 (26.17–28.46)	0.53
Preprocedural MoCA (mean ± SD; 95%CI)	22.9 ± 4.88 (19.86–25.91)	22.4 ± 3.57 (19.42–25.47)	0.83
Postprocedural MoCA (mean ± SD; 95%CI)	24.3 ± 4.77 (21.17–27.49)	25.3 ± 4.11 (22.17–28.49)	0.64
Basal S100B (mean ± SD; 95%CI)	0.0548 ± 0.0167 (0.0485–0.0611)	0.0529 ± 0.0172 (0.0466–0.0592)	0.68
2 h S100B (mean ± SD; 95%CI)	0.0617 ± 0.0217 (0.054–0.0695)	0.0605 ± 0.02 (0.0528–0.0683)	0.83
12 h S100B (mean ± SD; 95%CI)	0.0686 ± 0.0321 (0.0585–0.0786)	0.0657 ± 0.0206 (0.0557–0.0758)	0.69
24 h S100B (mean ± SD; 95%CI)	0.0785 ± 0.0442 (0.0649–0.0921)	0.071 ± 0.0265 (0.0575–0.0846)	0.44
48 h S100B (mean ± SD; 95%CI)	0.09 ± 0.0617 (0.0719–0.108)	0.082 ± 0.0302 (0.0639–0.1001)	0.53
Basal NSE (mean ± SD; 95%CI)	6.18 ± 1.87 (5.49–6.85)	5.86 ± 1.78 (5.18–6.54)	0.52
2 h NSE (mean ± SD; 95%CI)	6.46 ± 1.75 (5.82–7.09)	6.41 ± 1.67 (5.77–7.04)	0.9
12 h NSE (mean ± SD; 95%CI)	6.39 ± 1.53 (5.75–7.02)	6.18 ± 1.87 (5.54–6.81)	0.64
24 h NSE (mean ± SD; 95%CI)	6.07 ± 1.67 (5.47–6.66)	6.39 ± 1.53 (5.79–6-98)	0.45
48 h NSE (mean ± SD; 95%CI)	5.86 ± 1.78 (5.22–6.50)	6.07 ± 1.67 (5.42–6.71)	0.65
Increased S100B (n;%)*	22 (75.8%)	21 (72.4%)	0.76 (1.19; 0.36–3.88)
48 h increased S100B (n;%)°	26 (89.6%)	21 (72.4%)	0.09 (3.3; 0.77–14.02)
Increased NSE (n;%)*	11 (37.9%)	9 (31%)	0.58 (1.35; 0.45–4.02)
48 h increased NSE (n;%)°	13 (44.8%)	15 (51.7%)	0.59 (0.75; 0.27–2.12)

h: hour; DWMRI: diffusion-weighted magnetic resonance cerebral imaging; pt.: patient; MMSE: Mini-Mental State Examination Test; MoCA: Montreal Cognitive Assessment Test; NSE: Neuron-Specific Enolase;*: in every patient variations of S100B and NSE have been analyzed comparing every value with the basal one so that every patient has been classified as belonging to "increased", "stable", or "decreased" category if a ≥25% variation was detected and neurobiomarker values have been analyzed as categorical variables; °: in every patient variations of S100B and NSE have been analyzed comparing the 48-hour value with the basal one so that every patient has been classified as belonging to "increased", "stable", or "decreased" category if a ≥25% variation was detected and neurobiomarker values have been analyzed as categorical variables.

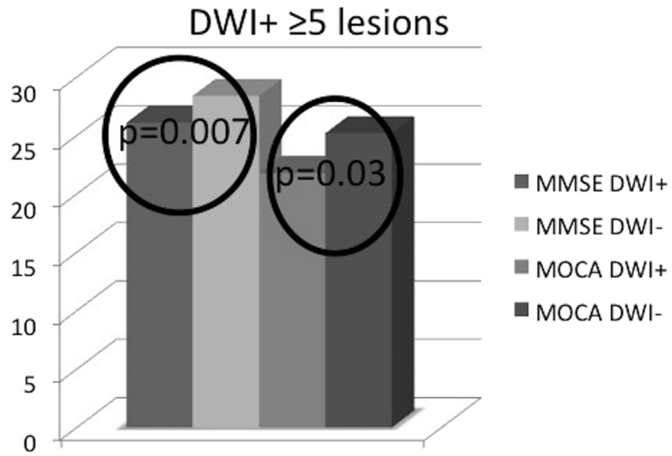

Fig. 2. 3PCAS postoperative MMSE and MoCA scores: NPTs postoperative scores showed a significant association with the presence of >5 DWMRI lesions, irrespective of lesion side ($p = 0.007$ and $p = 0.03$ for MMSE and MoCA, respectively).

S100B values doubled at 48 h postoperatively in 24 patients; among them 12 presented new DWMRI lesions; 48-h S100B increase was significantly related to 72-h DWMRI lesions ($p = 0.012$; Fig. 3).

One inguinal haematoma was recorded in each treatment group. One AMI occurred in CGuard patients.

4. Discussion

The new CGuard carotid stents have demonstrated a reduction in the post-procedural embolic effect during the carotid plaque healing period (considered as lasting up to 28–30 days after stent placement), with plaque coverage as small as 165 μm [11,12,26]. In contrast, in the present series there was no difference between the two stent groups during the peri-procedural period.

According to our study, a not-negligible number of bilateral or contralateral lesions were detected in both Wallstent and CGuard stent groups. Some authors [27] have demonstrated that during the procedure of CAS there are a high number of insulting maneuvers that are on average performed into the arch whenever a transfemoral CAS procedure is done. Aortic arch atherosclerotic disease is usually preoperatively evaluated by CT scans so that very "shaggy" aortas are commonly a reason to consider a different approach to the carotid bifurcation. In our study all patients were submitted to aortic arch and supraortic vessels CT evaluation to be enrolled for CAS, nevertheless the images obtained are probably not sensitive enough to demonstrate the capability of arch atherosclerosis to be affected by catheter and wire passage and movements that may dislodge microparticles to both brain hemispheres. Data collected in the present study probably reflect what happens into an arch commonly considered at low embolic risk when crossed by a guidewire. However, an interesting study on association between brain microemboli and clinical and subclinical consequences has demonstrated that under 200 μm those particles can be considered innocuous [28]. However, the possibility of embolism from the arch should be properly evaluated [29], since it might not be prevented by the use of CGuard vs Wallstent (nor other current carotid stent), not even completely prevented from the intraprocedural use of EPDs, nor eliminated from the flow-reversal systems with femoral access. However, the use of flow-reversal protection systems may be considered safer during the procedure [30], while the use of cervical systems might be considered protective from peri-procedural arch plaque debris detachments.

The Safety and Efficacy Study for Reverse Flow Used During Carotid Artery Stenting Procedure (ROADSTER) multicenter trial published results on the use of ENROUTE Trans-carotid NPS (Silk Road Medical Inc., Sunnyvale, Calif), a transcarotid neuroprotection system that warrants direct surgical common carotid access and cerebral embolic protection with high-rate flow reversal in CAS [30]. The innovative concept at the basis of this device is the possibility of applying a flow reversal filter directly in the common carotid artery, thus allowing for intraoperative debris to be averted from brain circulation, and avoiding crossing the arch and dislodging arch microemboli in the early postoperative period.

To further support the hypothesis that the majority of microemboli detected by our study are not from the carotid plaque, rather from the main access vessel, namely the arch, studies on cervical access employment during CAS – TCAR procedures – are extremely promising because they have demonstrated the ability to keep the number of embolic events to a minimum [8,30]. The possibility to combine complete carotid plaque coverage by the use of a mesh associated to a nitinol skeleton stent, and to completely avoid going through the risky arch, can be the future solution to reduce even the microembolic brain consequences. In our study the number of lesions was associated to both increase in biomarkers levels and in decrease in NPTs scores. Those data confirm previous studies concerning the effect of brain microembolic burden on cognitive performance in the peri-procedural period [5]. The use of biomarkers dosage or NPTs in CAS should once again be considered in major studies. The demonstration of extremely low major complication rates in prospective studies [2,4,8,10–13,25,30–32] should prompt the call for cognitive performance evaluation following any carotid revascularization procedure [33–35].

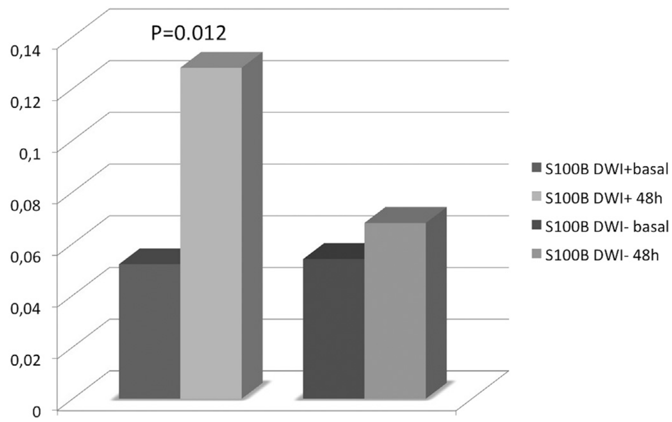

Fig. 3. 3PCAS postoperative lesions on DWMRI and S100B: analysis of basal and 48-hour S100B values in patients with new postoperative lesions (DWMRI +) and in patients without new postoperative lesions (DWMRI −).

5. Limitations

Despite its single-center nature, our study was able to provide the same technique, procedure, and materials in all patients, except for the kind of stent that was under investigation. This series represents our preliminary experience with the new mesh-covered stent, in contrast with the high experience gained in the use of Wallstent, so that some minor technical obstacles can't be excluded in the evaluation of results despite the adequate annual volume experience of the operators. Undoubtedly, clinical or subclinical relevance of peri-procedural DW-MRI lesions requires further evaluation.

6. Conclusions

In our experience both CGuard and Wallstent stents showed an acceptable rate of subclinical CAS-related neurological events with no significant differences at 72-hour DWMRI between groups. The rate of bilateral or contralateral lesions suggests that the peri-procedural neurological damage may have extra-carotid sources.

Acknowledgements

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