Clinical Outcomes of Second- versus First-Generation Carotid Stents: A Systematic Review and Meta-Analysis

Adam Mazurek 1,*†, Krzysztof Malinowski 2, Kenneth Rosenfield 3, Laura Capoccia 4, Francesco Speziale 4, Gianmarco de Donato 5, Carlo Setacci 5, Christian Wissgott 6, Pasqualino Sirignano 4, Lukasz Tekieli 7, Andrey Karpenko 8, Waclaw Kuczmik 9, Eugenio Stabile 10, David Christopher Metzger 11, Max Amor 12, Adnan H. Siddiqui 13, Antonio Micari 14, Piotr Pieniążek 1,7, Alberto Cremonesi 15, Joachim Schofer 16, Andrej Schmidt 17 and Piotr Musialek 1,*‡ on behalf of CARMEN (CArotid Revascularization Systematic Reviews and Meta-analyses) Investigators

1 Department of Cardiac and Vascular Diseases, John Paul II Hospital, Jagiellonian University, 31-202 Krakow, Poland
2 Department of Bioinformatics and Telemedicine, Faculty of Medicine, Jagiellonian University Medical College, 31-008 Krakow, Poland
3 Vascular Surgery, Surgery Department, Massachusetts General Hospital, Boston, MA 02114, USA
4 Vascular and Endovascular Surgery Unit, Department of Surgery, Sapienza University of Rome, 00185 Rome, Italy
5 Department of Vascular Surgery, University of Siena, 53100 Siena, Italy
6 Institut für Diagnostische und Interventionelle Radiologie/Neuroradiologie, Imland Klinik Rendsburg, 24768 Rendsburg, Germany
7 Department of Interventional Cardiology, John Paul II Hospital, Jagiellonian University, 31-202 Krakow, Poland
8 Centre of Vascular and Hybrid Surgery, E.N. Meshalkin National Medical Research Center, 630055 Novosibirsk, Russia
9 Department of General, Vascular Surgery, Angiology and Phlebology, Medical University of Silesia, 40-055 Katowice, Poland
10 Division of Cardiology, AOR San Carlo, 20123 Potenza, Italy
11 Wellmont CVA Heart and Vascular Institute, Kingsport, TN 37660, USA
12 Department of Interventional Cardiology, U.C.C.I. Polyclinique d’Essey, 54270 Nancy, France
13 Department of Neurosurgery, SUNY University at Buffalo, Buffalo, NY 14203, USA
14 Department of Biomedical and Dental Sciences and Morphological and Functional Imaging, University of Messina, 98122 Messina, Italy
15 Cardiovascular Department, Humanitas Gavazzeni Hospital, 24125 Bergamo, Italy
16 MVZ-Department Structural Heart Disease, Asklepios Clinic St. Georg, 20099 Hamburg, Germany
17 Department of Angiology, University Hospital Leipzig, 04103 Leipzig, Germany
* Correspondence: mazurekadam@yahoo.pl (A.M.); pmusialek@szpitaljp2.krakow.pl (P.M.)
† CARMEN Investigators Membership are provided in the Supplementary Material.

Abstract: Background: Single-cohort studies suggest that second-generation stents (SGS; “mesh stents”) may improve carotid artery stenting (CAS) outcomes by limiting peri- and postprocedural cerebral embolism. SGS differ in the stent frame construction, mesh material, and design, as well as in mesh-to-frame position (inside/outside). Objectives: To compare clinical outcomes of SGS in relation to first-generation stents (FGSs; single-layer) in CAS. Methods: We performed a systematic review and meta-analysis of clinical studies with FGSs and SGS (PRISMA methodology, 3302 records). Endpoints were 30-day death, stroke, myocardial infarction (DSM), and 12-month ipsilateral stroke (IS) and restenosis (ISR). A random-effect model was applied. Results: Data of 68,422 patients from 112 eligible studies (68.2% men, 44.9% symptomatic) were meta-analyzed. Thirty-day DSM was 1.30% vs. 4.11% (p < 0.01, data for SGS vs. FGS). Among SGS, both Casper/Roadsaver and CGuard reduced 30-day DSM (by 2.78 and 3.03 absolute percent, p = 0.014; DSM 1.3% vs. 3.15%, p < 0.01). At 12 months, in relation to FGS, Casper/Roadsaver reduced IS (−3.25%, p < 0.05) but increased ISR (+3.19%, p = 0.04), CGuard showed a reduction in both IS and ISR (−3.13%, −3.63%; p = 0.01, p < 0.01), whereas the Gore stent was neutral. Conclusions: Pooled SGS use was associated with improved short- and long-term clinical outcomes compared with FGS. Moreover, SGSs significantly improved outcomes compared with FGS (30-day stroke −2.78% vs. 3.03%, p < 0.01; DSM 1.3% vs. 3.15%, p < 0.01; IS 3.63% vs. 2.32%, p = 0.014; ISR 3.13% vs. 3.63%, p < 0.01).
results of CAS. Individual SGS types, however, differed significantly in their outcomes, indicating a lack of a “mesh stent” class effect. Findings from this meta-analysis may provide clinically relevant information in anticipation of large-scale randomized trials.

**Keywords:** carotid artery stenting; systematic review and meta-analysis; stent design; “mesh-covered” dual-layer stents; stroke prevention

### 1. Introduction

Carotid artery stenting (CAS) is established as an important minimally invasive treatment modality in primary and secondary stroke prevention in atherosclerotic carotid artery disease. Meta-analyses of large-scale randomized trials of first-generation (single-layer) stent CAS versus surgery (carotid endarterectomy, CEA) demonstrated equipoise of the two treatment modalities in long-term outcomes. Nevertheless, FGS CAS has been associated with a higher rate of ipsilateral neurologic events (mainly minor strokes) than CEA [1,2]. A significant proportion of these events (∼30–60%) occurs in the postprocedural period [3–6] and has been linked to plaque prolapse through the stent struts, triggering cerebral embolism [7,8]. Although neuroprotection devices may reduce CAS embolism during the procedure [9–11], the brain is no longer protected against embolism after the protection device is removed [7,9–12]. After the procedure the stent plays the role of a fundamental mechanistic protector against plaque-related adverse events. Single-layer closed-cell stent design may be associated with cerebral embolism resulting from plaque prolapse [3,13–15].

Today, effective plaque insulation has become a leading challenge in carotid disease management using the endovascular route [15,16]. To minimize atherosclerotic plaque prolapses and reduce adverse neurologic events in CAS [16,17], mesh stents (second-generation stents, SGS) have been developed. “Mesh stents” are often considered a new “class” of carotid stents [17,18]. However, SGS show fundamental differences in (i) the stent nitinol frame construction (closed-cell in Casper/Roadsaver, open-cell in CGuard and Gore stent), (ii) mesh material (nitinol in Casper/RoadSaver, polyethylene terephthalate in MicroNet-covered CGuard stent), mesh design (braided in Casper/Roadsaver, fenestrated in Gore stent, knitted in CGuard), and (iv) the mesh position in relation to the stent frame (stent frame wrapped with mesh in the Gore and CGuard stent, the mesh placed inside the frame in Casper/RoadSaver) [19–22].

Recently, several single-cohort studies [20,23–25] and two randomized studies [26,27] indicated that SGS may improve CAS outcomes by limiting peri- and postprocedural embolism. However, a pilot analysis suggested that SGS may differ in their clinical outcomes [28,29]. A systematic evaluation of SGS clinical events in comparison with FGS is lacking.

We performed a systematic review and meta-analysis of clinical outcomes with SGS in relation to FGS.

### 2. Methods

CAS studies with relevance to contemporary clinical practice were considered from the point of SAPHIRE [30]. For recent studies, an 24-month period was taken from the point of 30-day data publication to capture any releases of 12-month outcomes (Figure 1).

#### 2.1. Endpoints of Interest Identification

First, we assessed the clinical endpoints reported in CAS studies. A study statistician randomly identified (PubMed) 50 CAS studies reporting 30-day clinical outcomes [20,23,31–78] and 50 studies reporting 12-month clinical outcomes ([11,30,35,38,39,42,45,47,48,51–54,57,61, 62,64,66,68,69,79–108]). Typically reported 30-day clinical endpoints were death (D), any stroke (S), and myocardial infarction (MI) (Figure S1A), whereas most frequently reported
1-year endpoints were ipsilateral stroke (IS) and in-stent restenosis (ISR; Figure S1B). Those endpoints were further used for data comparisons.

**CARMEN Systematic review and meta-analysis flowchart (PRISMA)**

![Flowchart](image)

Figure 1. Meta-analysis flowchart. Preferred Reported Items for Systematic Reviews and Meta-Analysis (PRISMA) flowchart for studies reporting clinical outcomes of FGS and/or SGS in CAS. FGS—first-generation stent(s); SGS—second-generation stent(s); CAS—carotid artery stenting.

### 2. Methods

CAS studies with relevance to contemporary clinical practice were considered from the point of SAPPHIRE [30]. For recent studies, an 24-month period was taken from the point of 30-day data publication to capture any releases of 12-month outcomes (Figure 1).

#### 2.1. Endpoints of Interest Identification

First, we assessed the clinical endpoints reported in CAS studies. A study statistician randomly identified (PubMed) 50 CAS studies reporting 30-day clinical outcomes.

#### 2.2. Data Search and Initial Screening

PubMed, EMBASE, and COCHRANE Library were searched for publications (1 October 2004 and 31 October 2019) using the words “carotid” + “stent” + “trial” [or] “study.” Reference lists of the identified publications were checked to capture studies not identified in the initial search, and cross-references were also used. PRISMA methodology [109] and the CADIMA tool for systematic reviews and meta-analysis [110] were applied by two independent investigators working together. Typical systematic review...
steps were taken, including (1) identification, (2) screening (CADIMA, full-text English language papers published in peer-reviewed journals; Figure S2), (3) eligibility check, and (4) quality assessment (Figure 1). The study was registered with the PROSPERO database of systematic reviews (CRD42022339789).

2.3. Study Eligibility and Quality Assessment

Studies eligible for screening needed to satisfy the criteria of at least 30 subjects, de novo atherosclerosis, extracranial carotid procedure, elective carotid procedure, and unselected population (Figure S2). Both prospective (observational and randomized) and retrospective studies were considered.

A total of 3325 records were initially identified. Of these, 3308 records (17 duplicates eliminated) were introduced to CADIMA. Besides the initial screening criteria, the following requirements were applied: (1) publication in English, (2) original study publication, (3) human subjects, (4) stenosis $\leq$ 99%, (5) transfemoral access, and (6) not a substudy of a previously published study; this led to 736 records. Data flow through the CADIMA tool is presented in Figure S2. Studies reporting the endpoints of interest ($n = 149$) were taken for further analysis. Quality assessment was performed to identify bias in at least one of five bias categories (patient selection/recruitment, performance in relation to study device(s), performance other than in relation to study device(s), outcome detection, and attrition and reporting; Figure S3). Severe bias presence led to study exclusion from further analysis. Finally, CAS data from 103 observational and 9 randomized studies were included [4,21–23,26,27,30,35,39,41,44,45,56,58,65,66,84,89,91,92,97,104,111–224].

2.4. Data Extraction

Data were extracted by two investigators working together using a predefined data extraction form. In case of disagreement, a third investigator reviewed the publication(s) pertaining to a given study, and a consensus was reached.

2.5. Data Synthesis

The baseline demographics and outcomes were extracted. In the case of more than one publication referring to 30-day or 12-month outcomes from a particular study, the data were integrated.

2.6. Statistical Analysis

Clinical characteristics of patients enrolled in meta-analyzed studies are provided as counts and percentages and (weighted) proportions for nominal variables and means with standard deviations for continuous variables. Endpoints of interest are presented as counts as well as risk ratios (95%CI) for between-group comparisons. Raw, untransformed proportions were analyzed using the DerSimonian–Laird random-effect model. The influence of covariates was assessed using metaregression. Meta-analysis results were presented as forest plots with RR (CI) for SGS (and components) compared with FGS. Publication bias was assessed using funnel plots accompanied by Egger’s regression test for asymmetry. Heterogeneity among meta-analyzed studies was presented as a fraction of variance due to heterogeneity ($I^2$) and an estimate of the between-study variance ($\tau^2$) with $p$-value of a Q test. The continuity correction for zero-event arms was applied where applicable. Statistical analyses were performed using R v.4.1.1 (The R Foundation for Statistical Computing; https://www.r-project.org) with the “meta” package v.5.1.

3. Results

3.1. Eligible Trials and Results Display

Three-step screening followed by eligibility assessment of each record revealed 112 studies [4,21–23,26,27,30,35,39,41,44,45,56,58,65,66,84,89,91,92,97,104,111–224] with a total of 68,422 patients (68.2% men, 44.9% symptomatic) (Figure 1). Clinical characteristics
of the patient groups in respective stent categories (FGS, SGS, and FGS separated into open-cell and closed-cell single-layer stents) are presented in Table 1.

Table 1. Clinical characteristics of meta-analyzed groups.

|                      | FGS | SGS | FGS vs. SGS | Open-Cell FGS | Closed-Cell FGS | FGS vs. Closed-Cell FGS | FGS vs. SGS |
|----------------------|-----|-----|-------------|---------------|-----------------|-------------------------|-------------|
| No. of studies       | 98  | 14  | -           | 29            | 12              | -                       | -           |
| No. of patients      | 65,891 | 2531 | -           | 21,351        | 7598            | -                       | -           |
| Age (SD)             | 70.1 (2.8) | 71.9 (2.5) | 0.02        | 70.4 (3.2)    | 69.3 (3.4)      | 0.60                    | 0.32        |
| Male                 | 68% | 73% | 0.046       | 68%           | 66%             | 0.92                    | 0.12        |
| Symptomatic          | 45% | 41% | 0.40        | 43%           | 50%             | 0.61                    | 0.94        |
| Diabetic             | 34% | 32% | 0.43        | 35%           | 36%             | 0.71                    | 0.88        |
| CAD                  | 51% | 47% | 0.55        | 48%           | 55%             | 0.59                    | 0.98        |
| AF                   | 6%  | 3%  | 0.37        | 3%            | ND              | -                       | 0.99        |
| Contralateral occlusion | 10% | 16% | 0.22        | 10%           | 12%             | 0.87                    | 0.63        |
| Embolic protection in CAS | 95.8% | 97.1% | 0.656       | 97.3%         | 99.4%           | 0.09                    | 0.85        |

Data are shown as absolute number, mean (SD), or weighted proportion (%) as appropriate.

Clinical event rates (i.e., combined and individual stent-type DSM at 30 days and combined and individual 12-month IS/ISR) according to the meta-analytic model are given in Table 2. Data are given for (i) FGS vs. pooled SGS and (ii) FGS vs. each individual SGS, i.e., Casper/Roadsaver (CR), Gore stent (GS), and CGuard MicroNet-covered stent (CG). Table 3 provides a comparison of the \( p \)-values. The 30-day and 12-month relative outcomes for fundamental comparisons are provided in the Figure 2. Figure 3 shows the 30-day SGS outcome comparisons against the open- and closed-cell single-layer stents. The combined 12-month IS/ISR for SGS vs. FGS is presented in the Supplementary Materials (Figure S4). Funnel plots are provided in Figures S5 and S6.

Table 2. The 30-day and 12-month event rates by stent type (random-effect model).

|                      | FGS | SGS | Casper/Roadsaver | Gore | CGuard |
|----------------------|-----|-----|------------------|------|--------|
| 30-day Stroke (%)    | 3.01| 0.60| 0.50             | 2.89 | 0.54   |
| (95% CI)             | (2.63–3.38) | (0.28–0.92) | (0–1.15) | (1.03–4.76) | (0.17–0.92) |
| 30-day Death/Stroke/MI (%) | 4.11| 1.30| 1.33             | 4.82 | 1.08   |
| (95% CI)             | (3.65–4.56) | (0.64–1.96) | (0–2.66) | (2.44–7.2) | (0.55–1.60) |
| 12-mo Ipsilateral Stroke (%) | 3.51| 0.7 | 0.26             | 3.1  | 0.38   |
| (95% CI)             | (2.52–4.50) | (0–1.47) | (0–1.27) | (1.11–5.1) | (0–0.9) |
| 12-mo Restenosis (%) | 3.97| 3.38| 7.16             | 4.83 | 0.34   |
| (95% CI)             | (2.8–5.14) | (1.39–5.37) | (5.45–9.86) | (2.36–7.29) | (0–0.82) |
| 12-mo Ipsilateral Stroke/Restenosis (%) | 8.15| 5.12| 7.86             | 7.93 | 0.73   |
| (95% CI)             | (6.63–9.96) | (3.14–6.10) | (5.04–10.68) | (4.82–11.04) | (0–1.44) |
Table 3. The p-values for 30-day and 12-mo SGS event rate comparisons against FGS (for the meta-analytic model raw event rates, see Table 2).

|                      | FGS vs. SGS | FGS vs. Roadsaver | FGS vs. Gore | FGS vs. CGuard |
|----------------------|-------------|-------------------|--------------|----------------|
| **30-day Stroke**    | <0.001      | 0.011             | 0.954        | 0.002          |
| **Death/Stroke/MI**  | <0.001      | 0.022             | 0.750        | <0.001         |
| **12-mo Ipsilateral Stroke** | 0.001 | 0.007             | 0.846        | 0.013          |
| **12-mo Restenosis** | 0.569       | 0.041             | 0.658        | 0.009          |
| **12-mo Ipsilateral Stroke/Restenosis** | 0.027 | 0.998             | 0.961        | 0.001          |

3.2. Quality Assessment and Risk of Bias

A severe bias in at least one category, leading to study exclusion, was identified in 21 out of 133 studies (15.9%; Figure S3A). Severe bias occurred in the following categories (in order of prevalence): (i) patient selection/recruitment, (ii) outcome detection, (iii) performance unrelated to the study device, (iv) performance in relation to the study device(s), and (v) attrition and reporting (respectively 57.1%, 28.6%, 14.3%, 9.6%, and 9.6% of rejected studies; Figure S3B). Severe bias in two or more categories occurred in four (19%) rejected studies.

The overall quality of 112 included studies was moderate. Moderate bias in at least one category was present in 102 (91%) studies and in two or more categories in 64 (57%) studies (Figure S3C–E). There were 10 studies (9%) with mild or absent bias in all categories.

3.3. 30-Day Outcomes: SGS vs. FGS

According to the meta-analytic model, the 30-day death, stroke, and MI rate (DSM) for FGS was 4.11% (Table 2). The 30-day FGS stroke rate was 3.01% (Table 2). Pooled SGS showed a markedly lower 30-day event rate (DSM 1.30%, stroke 0.6%, absolute reduction by 2.81% and 2.41%, respectively, p < 0.001 vs. FGS for both; RR's and 95% CIs are given in forest plots). Individual SGS 30-day event rates were the following: CR-DSM 1.33% (p = 0.02 vs. FGS, absolute reduction by 2.78%), CG-DSM 1.08% (p < 0.001 vs. FGS, absolute reduction by 3.03%), GS-DSM 4.82% (p = 0.75 vs. FGS, absolute increase by 0.71%). The 30-day stroke rate was 0.5% with CR (p = 0.01 vs. FGS, absolute reduction by 2.51%), 2.89% with GS (p = 0.95 vs. FGS, absolute reduction by 0.12%), and 0.54% with CG (p = 0.002 vs. FGS, absolute reduction by 2.47%). The Figure 2 forest plots A and B demonstrate the 30-day relative outcomes for SGS as a group vs. FGS as well as individual SGS (CR, CG, GS) outcomes in relation to FGS.

3.4. 12-Month Outcomes: SGS vs. FGS

The 12-month IS rate for FGS was 3.51%. The 12-month IS rate for FGS was 3.97% (Table 2). Pooled SGSs showed a markedly lower 12-month IS rate (0.7%, absolute reduction by 2.81%, p = 0.001) but not ISR reduction (3.38%, absolute reduction by 0.59%, p = 0.57).

Individual 12-month SGS event rate analysis revealed significant differences between the SGS types. CR-IS is 0.26% (p = 0.007 vs. FGS, absolute reduction by 3.25%) and CG-IS 0.38% (p = 0.013 vs. FGS, absolute reduction by 3.13%), GS-IS 3.1% (p = 0.846 vs. FGS, absolute reduction by 0.41%). The individual 12-month SGS IS rate was 7.16% with CR (p = 0.04 vs. FGS, absolute increase by 3.19%), 4.83% with GS (p = 0.66 vs. FGS, absolute increase by 0.86%), and 0.34% with CG (p = 0.009 vs. FGS, absolute reduction by 3.63%). Figure 2 forest plots C and D show the 12-month relative outcomes for SGS taken as a group and for individual SGS stent brands in relation to FGS.
The 12-month combined endpoint of IS and ISR (Table 2; Figure S4) was reduced with SGSs taken as a group by 3.03% (FGS 8.15%, SGS 5.12%, \( p = 0.027 \)). Individual SGS evaluation showed a significant reduction in IS/ISR only with CG (combined event rate 0.73%, reduction by 7.42% vs. FGS, \( p = 0.001 \)). In contrast, CR and GS did not reduce 12-month IS/ISR against FGS (−0.29% and −0.22%; \( p = 0.99 \) and \( p = 0.96 \), respectively). In CR, the lack of a significant reduction in the 12-month combined endpoint was driven by an increase in ISR that offset the relative benefit in IS (Table 2; Figures 2 and S4). For GS, the increase in combined IS/ISR (Figure S4) occurred as a result of an increase in both composites of the combined 12-month endpoint (Table 2).

### 3.5. FGS Stent Type: Open- vs. Closed-Cell Design

SGS 30-day outcome comparisons against open- and closed-cell FGS are shown in Figure 3. According to the meta-analytic model, the 30-day DSM for open-cell FGS was
4.18%, whereas for closed-cell FGS, it was 3.15%; these were reduced with SGS by 2.88% ($p < 0.001$) and 1.85% ($p = 0.005$), respectively. The 30-day stroke rate was 3.15% for open-cell FGS and 2.32% for closed-cell FGS (reduction with SGS respectively by 2.55%, $p < 0.001$; and 1.72%, $p = 0.005$). Thirty-day DSM comparisons for individual SGS brands against open-cell FGS showed the following: an absolute reduction of 2.85% for CR ($p = 0.004$), a nonsignificant absolute increase by 0.64% for GS ($p = 0.73$), and an absolute 3.1% for CG ($p < 0.001$). Thirty-day DSM comparisons for individual SGS brands against closed-cell FGSs showed an absolute reduction by 1.82% for CR ($p = 0.030$), an absolute increase by 1.67% for GS ($p = 0.031$), and an absolute reduction by 2.07% for CG ($p = 0.003$).

![Figure 3](image-url)  
**Figure 3.** SGS 30-day clinical outcomes in relation to open-cell FGS (A,B) and closed-cell FGS (C,D) used as a reference. The forest plots include the data of 28,274 patients in studies with clinical outcomes available according to FGS stent design (i.e., open- or closed-cell FGS, left and right panel, respectively) that are used here as a reference for the SGS relative benefit/harm. SGS as a group ($n = 28,274$) showed a benefit in 30-day stroke and 30-day death/stroke/MI relative risk reduction in relation to not only open- (A,B) but also closed-cell FGS (C,D). Note that this effect was driven by the Casper/Roadsaver and C-Guard MicroNet stents, whereas the Gore Mesh stent was neutral in relation to open-cell FGS but came out inferior in comparison to closed-cell (see text for details). For respective funnel plots, see Supplementary Figure S5. FGS, first-generation stent(s); SGS, second-generation stent(s).

Thirty-day stroke rate comparisons for individual SGS against closed-cell FGS showed an absolute reduction of 2.65% for CR ($p = 0.001$), a nonsignificant reduction by an absolute 0.26% for GS ($p = 0.88$), and an absolute reduction by 2.61% for CG ($p < 0.001$). Thirty-day stroke rate comparisons for individual SGS against closed-cell FGS showed a reduction by 1.82% for CR ($p = 0.02$), an increase by 0.57% for GS ($p = 0.036$), and a reduction by 1.78% for CG ($p = 0.01$).

Overall, SGS individual and group 30-day outcomes were consistent irrespective of open- or closed-cell FGS use as a comparator. There were not enough studies reporting 12-month outcomes of open- and closed-cell FGS to enable a separate 12-month clinical endpoint evaluation of SGS in relation to open- and closed-cell FGS.

3.6. SGS Stent Brand Comparisons

The comparison of 30-day and 12-month outcomes within the SGS group revealed marked differences between the individual SGS representatives (Table 2). The 30-day
DSM and stroke rate were similar between CR and CG (1.33% and 1.08%, nonsignificant increase in CG of 0.25%, \( p = 0.37 \)). GS, however, showed an increase in 30-day DSM (4.82%) compared with both CR (significant increase of 2.39%, \( p = 0.001 \)) and CG (significant increase of 2.35%, \( p = 0.01 \)). The 30-day stroke rate was not different between CR and CG (0.50% and 0.54%, respectively, nonsignificant increase in CG of 0.04%, \( p = 0.899 \)), but was significantly higher in GS compared with both CR and CG (2.89%; an increase by an absolute 2.39% and 2.35%, \( p = 0.017 \) and \( p = 0.045 \), respectively).

The 12-month IS/ISR rate in CG (0.73%) was significantly lower than in CR or GS (7.86% and 7.93%; reduction by an absolute 7.13% vs. CR and by 7.20% vs. GS; \( p < 0.001 \) and \( p = 0.01 \), respectively). There was no difference in the 12-month IS/ISR between CR and GS (nonsignificant reduction by 0.07% for CR, \( p = 0.80 \)). This was driven by a significantly lower 12-month ISR in CG (0.34%) in relation to CR (7.16%, reduction of 6.82%, \( p < 0.001 \)) and GS (4.83%, reduction of 4.49%, \( p = 0.01 \)) and no difference between CR and GS (ISR reduction with GS against CR by 2.33%, which did not reach statistical significance, \( p = 0.34 \)). The 12-month IS rate was similar for CR and GS (0.26% and 0.38%, \( p = 0.717 \)) but was higher in GS (3.1%, a significant increase by an absolute 2.84% vs. CR, \( p = 0.014 \); and an increase by an absolute 2.72% with GS vs. CG; Table 2).

### 3.7. Heterogeneity

There was considerable heterogeneity among the analyzed studies and the outcomes of interest (\( I^2 > 70\% \) for all outcomes), prompting the use of a random-effect meta-analytic model. Heterogeneity evaluation using the Q test was concordant (\( p < 0.01 \) for all analyzed studies/outcomes). Funnel plots are provided in Figure S5.

### 4. Discussion

The fundamental findings from this systematic review and meta-analysis comparing second-generation (“mesh stent”) against first-generation (single metallic layer stent) are the following: (1) The 30-day death/stroke/MI rate were significantly reduced with SGS, an effect driven predominantly by a reduction in peri- and postprocedural strokes with CGuard and Casper/Roadsaver. (2) Among the SGSs, both Casper/Roadsaver and CGuard reduced the 30-day DSM and stroke rates, whereas the Gore stent was neutral. (3) SGS showed superiority also when compared with closed-cell FGS, including a nearly four-fold reduction in 30-day strokes. (4) At 12 months, in relation to FGS, Casper/Roadsaver reduced IS but increased ISR, CGuard showed a reduction in both IS and ISR, and the Gore stent was neutral.

The stent in carotid artery intervention plays a unique role in that after the embolic protection system has been removed, the stent is the main line of defense (along with antiplatelet therapy) against embolic and thromboembolic complications that may arise from the newly remodeled plaque with the varying degree of plaque coverage dependent on the stent design [225].

This work was undertaken to generate information with respect to patient outcomes that are relevant in routine clinical practice. Today, clinicians are exposed to often contradictory data regarding strategies in carotid revascularization in primary and secondary stroke prevention. Within the limitations that need to be taken into account (see below), the data from this systematic review and meta-analysis may play a role in informing clinical decisions until larger sets of randomized evidence [27] become available.

There was a considerable heterogeneity among the analyzed studies and the outcomes of interest (\( I^2 > 70\% \), \( p < 0.01 \) in Q test). Although a lower level of heterogeneity would be considered optimal for overall data interpretation, what this work found is a reflection of reality as per a rigorous process of data identification and quality assessment. Several factors may contribute to high heterogeneity within the pool of CAS data available today. These include differences in study populations, different specialties performing the procedures (resulting in differences in patient selection for CAS), differences in study design (such as randomized or single cohort), some changes in clinical guidelines and definitions over time,
and evolution in pharmacotherapy and medical equipment used in CAS. All those may be relevant to this analysis even if we have not taken into consideration data from before the SAPPHIRE study [30] that may have less relevance to contemporary clinical practice.

Overall, the heterogeneity level of studies in this systematic review and meta-analysis is considered to reflect the large spectrum of patients treated with CAS, with variations in the proportions of symptomatic and asymptomatic patients.

Indexes of data heterogeneity in this meta-analysis prompt caution in interpreting the results. Nonetheless, when considering the relevance of this work to clinical decision-making, it is important to note that the event rates in upcoming studies of FGS and SGS are broadly concordant with the event rates indicated in this meta-analysis (Table 2). Contemporary FGS data in the ACST-2 trial CAS arm (1811 patients with asymptomatic carotid stenosis, >98% FGS use) show the 30-day DSM of 3.9% (30-day stroke rate, 3.6%) [226].

Most recent an upcoming studies show event rates consistent with the meta-analytic model. Regarding SGS, the most recent Casper/Roadsaver and CGuard data show 30-day and 12-month event rates consistent with those indicated by the meta-analytic model. Some exception is the 30-day DSM with Casper/Roadsaver; that in some reports, appears to be higher than indicated on the basis of initial data sets. Specifically, in a recent study of 287 patients implanted with Casper/Roadsaver, there were nine strokes by 30 days (3.1%), including three postprocedural ischemic strokes (two due to stent thrombosis) [227], a rate greater than that indicated by our random-effects model (Table 2). Regarding 12-month outcomes with Casper/Roadsaver, recent multicentric data from Japan show an ISR rate of 8.5% and a 12-month IS/ISR rate of 9.9% [228], consistent with the rate determined by this meta-analysis (7.86, 95%CI 5.04–10.68; Table 2). Another very recent study reported a Casper/Roadsaver ISR rate of 8.2% at 12 months that further increased to 13.3% at 2 years [229].

Upcoming data regarding the real-life performance of the CGuard stent are consistent with the findings from this meta-analysis. In 103 patients recently treated with CGuard, no DSM occurred by 30 days [230]. A very recent 733-patient multicentric (20 centers) CGuard study in Italy showed three strokes by 30 days (0.4%, cumulative DSM rate of 0.95%) [231] and a 12-month ISR rate of 0.82% [232]. These outcomes are consistent with those indicated by the meta-analytic model (Table 2). As the Gore mesh stent has not been marketed, data other than captured in this systematic review are not available.

What is needed next is (i) to rigorously compare SGS outcomes against contemporary surgery and the hybrid carotid revascularization technique of transcarotid revascularization (TCAR) using a conventional (single-layer) carotid stent and (ii) to evaluate long-term outcomes with SGSs [178]. SGS comparisons against contemporary carotid endarterectomy that shows a 30-day DSM of ≈1.9% [233] is particularly needed. Very relevant in the context of the present analysis are the TCAR data, demonstrating that despite optimized intraprocedural cerebral protection, the use of FGS in TCAR is associated with a two-fold increase in early stroke/TIA in symptomatic vs. asymptomatic patients (2.5% vs. 1.2%, odds ratio 1.99, 95% CI 1.01–3.92, p = 0.046) [234]. This suggests that SGS plaque sealing might improve TCAR outcomes in symptomatic patients and high-risk lesions in particular [235]. Rigorous follow-up of SGS-implanted patients beyond 12 months is also needed [178,229,236].

5. Limitations

One fundamental limitation of this meta-analysis is a large disproportion between the volume of SGS vs. FGS data. This, however, is natural with any new technology that requires to be compared with a historical standard. Secondly, the majority of SGS studies were performed later than FGS studies; thus, the evolution of pharmacologic and interventional techniques (and experience of operators) might affect the outcomes. Third (and for the reasons above), this work is based mostly on single-arm studies and stent arm data from trials comparing CAS with surgery. Regrettably, no sufficient patient characteristics information was routinely provided to enable propensity matching. Fourth, relative differences in the volume of individual stent type (or brand) data published within...
the particular group(s) may contribute to the “direction” of the overall group data reflecting the largest component of the group. This may be relevant particularly for the SGS pooled results where individual stent type outcomes differ. While this cannot be corrected by matching the group volumes (as a systematic review of published data, by definition needs to include all studies that meet the search criteria), it is elucidated by providing individual SGS stent type comparisons – both against FGS (Figures 1 and 2) and among the SGS group (Table 2). Fifth, with >50,000 patients analyzed (112-studies), it was not feasible to obtain and process individual patient data [28,29]. Similarly, it was not possible to analyze the technical success rate (or procedural difficulties with any particular stent types), particularly as these (unfortunately) do not get routinely reported. Stent design-related differences, including the delivery profile and properties of the individual stent delivery systems, may play a practical role particularly for some less experienced operators. Sixth, there have been several changes in MI definition over time, possibly affecting the DSM endpoint in our analysis; this, however, would favor FGS rather than SGS. Seventh, consistent with prior analyses [235,237], there were not enough studies to analyze SGS 12-month outcomes against 12-month outcomes separately for open- and closed-cell single-layer stents. Eighth, although studies with a clear bias were excluded (21/133, 15.8%), the overall quality of the published data was found to be moderate. Finally, the findings from the present analysis may be affected by selective reporting and publication bias.

6. Conclusions

A systematic review and meta-analysis of available data indicates that SGS use may be associated with significantly better (than FGS) short- and long-term results of CAS, providing meta-analytic evidence for improvement in CAS outcomes with dual-layer stent technologies [238]. The SGS benefit is particularly relevant were both 30-day and 12-month rate of complications is reduced (Figure 2). An important finding is that the individual SGS types significantly differ (both in their outcomes related to FGS and for outcomes within the SGS group) indicating lack of any carotid ‘mesh-stent’ class effect. This work provides several clinically-relevant hypotheses for further testing in large randomized trials powered for clinical endpoints. However, in absence of large-scale randomized evidence at present, data from this systematic review and meta-analysis may inform clinical decision-making regarding device choices in percutaneous carotid revascularization.

7. Perspectives

7.1. What Is Known?

Several single-cohort studies have suggested that second-generation stents (SGS; “mesh stents”) may improve carotid artery stenting (CAS) outcomes by limiting peri- and inhibiting postprocedural cerebral embolism. A recent randomized controlled study demonstrated a profound reduction in periprocedural (and elimination of postprocedural) cerebral embolism with the MicroNet-covered stent in relation to a first-generation (FGS; single metallic layer) stent [27].

“Mesh stents” differ in the stent frame construction, mesh material, and design, as well as mesh-to-frame placement (mesh wrapping the stent frame vs. placed inside).

7.2. What Is New?

Our systematic review and meta-analysis of the clinical data of 68,422 patients (112 studies) treated using FGS or SGS demonstrated that outcomes at 30 days (death/stroke/MI) were significantly improved for pooled “mesh stents” in relation to FGSs. The benefit was present for SGSs against both open and closed-cell FGS. At 12 months, ipsilateral stroke and in-stent restenosis were significantly reduced with SGS. However, individual SGS significantly varied in their performance at 30-days and 12-months, indicating a lack of a “class” effect. This may be relevant for decision-making in primary and secondary stroke prevention with CAS in clinical practice.
7.3. What Is Next?

While upcoming studies of FGS and SGS show outcomes largely consistent with this meta-analysis, large-scale randomized controlled studies powered for clinical outcomes would be ideally desired for a rigorous prospective comparison of individual SGS types against FGS and against surgery.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm11164819/s1, Figure S1. Random Sample CAS Study Endpoints. (A) for 30-day endpoints \( (n = 50) \) and (B) for 12-month endpoints \( (n = 50) \); Figure S2. Study selection process: CADIMA systematic review and meta-analysis tool; Figure S3. Bias systematic assessment; Figure S4. Forrest-plot presenting meta-analytic data for the combined 12-month endpoint of ipsilateral stroke and restenosis. With FGS used as a reference, the benefit of Casper/Roadsaver in reducing 12-month ipsilateral stroke rate was neutralized by its relative harm—increased restenosis rate (for the individual endpoint data see Figure 2); Figure S5. Funnel plots of different stent type comparisons—30-day outcomes; Figure S6. Funnel plots of different stent type comparisons-12-monthly outcomes.

Author Contributions: Conception and design, A.M. (Adam Mazurek), K.R., A.S., A.M. (Antonio Micari) and P.M.; analysis of the data, A.M. (Adam Mazurek), K.M., G.d.D., L.T. and P.M.; interpretation of data, A.M. (Adam Mazurek), K.R., F.S., C.S., C.W., E.S., A.K., D.C.M., A.M. (Antonio Micari), A.C., W.K., A.S. and P.M.; drafting of the manuscript, A.M. (Adam Mazurek), L.C., A.H.S., K.M., P.S., M.A. and P.M.; manuscript revision for critical intellectual content, A.M. (Adam Mazurek), K.R., F.S., C.S., E.S., A.M. (Antonio Micari), A.C., A.H.S., A.S. and P.M.; final approval of the manuscript submitted, all CARMEN Investigators including A.M. (Adam Mazurek), K.M., K.R., L.C., F.S., G.d.D., C.S., C.W., P.S., L.T., A.K., W.K., E.S., D.C.M., M.A., A.H.S., A.M. (Antonio Micari), P.P., A.C., J.S., A.S. and P.M. All authors have read and agreed to the published version of the manuscript.

Funding: Jagiellonian University Research Grant No. K/ZDS/007819, N41/DBS/000822) and John Paul II Hospital in Kraków Research Fund.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: The studies included in this meta-analysis indicated that informed consent was received from all participants.

Data Availability Statement: Raw extracted data are available (on request) from the corresponding authors (A.M. and P.M.); statistical analysis details are available (on request) from the study statistician (K.M.).

Conflicts of Interest: Kenneth Rosenfield reports receiving fees for serving on advisory boards from Abbott Vascular, Cardinal Health, Surmodics, Inari Medical, Volcano/Philips, and Proteon; receiving fees and stock options for serving on advisory boards from Cruzar Systems, Valcare, and Eximo; receiving stock options for serving on advisory boards from Capture Vascular, Shockwave, Micell, Endospan, and Silk Road Vascular; receiving stock options for serving on the advisory boards of and the holding of equity positions in Contego, Access Vascular, and MD Insider; holding stock/stock options in Embolitech, Janacare, Primacea, and PQ Bypass; receipt of a future payout from a previous equity position in Vortex; and receiving grant support paid to his institution from Abbott Vascular, Atrium/Maquet, and Lutoxin/Bard. David Christopher Metzger is Co-Principal Investigator in the CGUARDIANS FDA-IDE Trial. Adnan H. Siddiqui has consulted for Amnis Therapeutics Ltd, Cerebrotech Medical, Systems Inc, CereVasc LLC, Claret Medical Inc, Codman, Corindus Inc, GuidePoint Global Consulting, Medtronic (Formerly Covidien), MicroVention, Neuravi, Penumbra, Pulsar Vascular, Rapid Medical, Rebound Therapeutics Corporation, Silk Road Medical, Stryker, The Stroke Project Inc, Three Rivers Medical Inc, W.L. Gore & Associates, and is a Board Member of Intersocietal Accreditation Commission. He has been Principal Investigator and/or served on Steering Committees for: Codman & Shurtleff, LARGE Trial, Coviden (Now Medtronic), SWIFT PRIME and SWIFT DIRECT Trials; MicroVention, FRED Trial, CONFIDENCE Study, MUSC, POSITIVE Trial; Penumbra, 3D Separator Trial, COMPASS Trial, INVEST Trial. AHS has financial interests in BuffaloTechnology Partners Inc, Cardinal, International Medical Distribution Partners, Medina Medical Systems, Neuro Technology Investors, StimMed, and Valor Medical. Piotr Pieniazek
has proctored and/or consulted for Terumo, Boston Scientific and Balt. Joachim Schofer has been Co-Principal Investigator in the CARENET Trial. Andrej Schmidt has consulted for Abbott Vascular, BD, Cook and Medtronic. Piotr Musialek has proctored and/or consulted for Abbott Vascular, InspireMD, and Medtronic. PM is Co-Principal Investigator in the CGUARDIANS FDA-IDE Trial and has been Co-Principal Investigator in the CARENET Trial; he is Principal Investigator in a series of Investigator-Initiated studies including PARADIGM/PARADIGM-Extend (NCT04271033), FLOW-GUARD (NCT04461717), OPTIMA (NCT04234854), TOP-GUARD (NCT0454738), C-HEAL (NCT04434456), SIM-GUARD (NCT04973579) and SAFEGUARD-STROKE (NCT05195658). PM is the Polish Cardiac Society Board Representative for Stroke and Vascular Interventions and serves on the European Society of Cardiology (ESC) Stroke Council Scientific Documents Task Force and on ESC Research and Grants Committee. Other author declare no conflict of interest.

Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| CADIMA       | Online evidence synthesis tool for the conduct and reporting of systematic reviews |
| CG           | CGuard MicroNet-covered carotid stent (laser-cut nitinol frame covered with PET micro-mesh sleeve) |
| DSM          | Death, stroke, myocardial infarction |
| FGS          | First-generation (single-layer) carotid stent(s) |
| GS           | Gore carotid stent (laser-cut nitinol frame covered by Teflon mesh layer) |
| IS           | Ipsilateral stroke |
| ISR          | In-stent restenosis |
| CR           | Casper/RoadSaver dual metallic layer carotid stent (braided metallic mesh inside the metallic, braided frame) |
| PRISMA       | Preferred Reporting Items for Systematic Review and Meta-Analysis |
| PROSPERO     | International Prospective Register of Systematic Reviews |
| SGS          | Second-generation (mesh-stent) carotid stent(s) |

References

1. Sardar, P.; Chatterjee, S.; Aronow, H.D.; Kundu, A.; Ramchand, P.; Mukherjee, D.; Nairooz, R.; Gray, W.A.; White, C.J.; Jaff, M.R.; et al. Carotid Artery Stenting Versus Endarterectomy for Stroke Prevention: A Meta-Analysis of Clinical Trials. *J. Am. Coll. Cardiol.* 2017, 69, 2266–2275. [CrossRef] [PubMed]
2. Brott, T.G.; Calvet, D.; Howard, G.; Gregson, J.; Algra, A.; Becquemin, J.-P.; de Borst, G.J.; Bulbulia, R.; Eckstein, H.-H.; Fraedrich, G.; et al. Long-term outcomes of stenting and endarterectomy for symptomatic carotid stenosis: A preplanned pooled analysis of individual patient data. *Lancet Neurol.* 2019, 18, 348–356. [CrossRef]
3. Bonati, L.H.; Jongen, L.M.; Haller, S.; Flach, H.Z.; Dobson, J.; Nederkoorn, P.J.; Macdonald, S.; Gaines, P.A.; Waaier, A.; Stierli, P.; et al. New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: A substudy of the International Carotid Stenting Study (ICSS). *Lancet Neurol.* 2010, 9, 353–362. [CrossRef]
4. Ikari, Y.; Misumi, K.; Yokoi, H.; Ogata, N.; Umemoto, T.; Usugi, M.; Kinoshita, Y.; Nakano, M.; Higashitani, M.; Abe, H.; et al. Initial results of carotid artery stenting in Japan. *Cardiovasc. Interv. Ther.* 2013, 28, 37–44. [CrossRef]
5. Fairman, R.; Gray, W.A.; Scici, A.P.; Wilburn, O.; Verta, P.; Atkinson, R.; Yadav, J.S.; Wholey, M.; Hopkins, L.N.; Raabe, R.; et al. The CAPTURE registry-Analysis of strokes resulting from carotid artery stenting in the post approval setting: Timing, location, severity, and type. *Ann. Surg.* 2007, 246, 551–556. [CrossRef]
6. Hill, M.; Brooks, W.H.; Mackey, A.; Clark, W.M.; Meschia, J.F.; Morrish, W.F.; Mohr, J.; Rhodes, J.D.; Popma, J.J.; Lal, B.K.; et al. Stroke after carotid stenting and endarterectomy in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). *Circulation* 2012, 126, 3054–3061. [CrossRef]
7. Kotsugi, M.; Takayama, K.; Myouchin, K.; Wada, T.; Nakagawa, I.; Nakagawa, H.; Taoka, T.; Kurokawa, S.; Nakase, H.; Kichikawa, K. Carotid Artery Stenting: Investigation of Plaque Protrusion Incidence and Prognosis. *JACC Cardiovasc. Interv.* 2017, 10, 824–831. [CrossRef]
8. Shinozaki, N.; Ogata, N.; Ikari, Y. Plaque protrusion detected by intravascular ultrasound during carotid artery stenting. *J. Stroke Cerebrovasc. Dis.* 2014, 23, 2622–2625. [CrossRef]
9. Paraskevas, K.I.; Mikhailidis, D.P.; Veith, F.J. Mechanisms to explain the poor results of carotid artery stenting (CAS) in symptomatic patients to date and options to improve CAS outcomes. *J. Vasc. Surg.* 2010, 52, 1367–1375. [CrossRef]
10. Montorsi, P.; Cabutti, L.; Galli, S.; Ciceri, E.; Ballerini, G.; Agrifoglio, M.; Ravagnani, P.; Trabattoni, D.; Pontone, G.; Fabbrioci, F.; et al. Microembolization during carotid artery stenting in patients with high-risk, lipid-rich plaque. A randomized trial of proximal versus distal cerebral protection. *J. Am. Coll. Cardiol.* 2011, 58, 1656–1663. [CrossRef]
11. Pieniazek, P.; Musialek, P.; Kablak-Ziembicka, A.; Tekieli, L.; Motyl, R.; Przewlocki, T.; Moczulski, Z.; Pasowicz, M.; Sokolowski, A.; Lesniak-Sobela, A.; et al. Carotid artery stenting with patient- and lesion-tailored selection of the neuroprotection system
and stent type: Early and 5-year results from a prospective academic registry of 535 consecutive procedures (TARGET-CAS). J. Endovasc. Ther. 2008, 15, 249–262. [CrossRef] [PubMed]

12. Schofer, J.; Arendt, M.; Tubler, T.; Sandstedt, J.; Schluter, M. Late cerebral embolization after emboli-protected carotid artery stenting assessed by sequential diffusion-weighted magnetic resonance imaging. JACC Cardiovasc. Interv. 2008, 1, 571–577. [CrossRef]

13. De Donato, G.; Setacci, F.; Sirignano, P.; Galzerano, G.; Cappelli, A.; Setacci, C. Optical coherence tomography after carotid stenting: Rate of stent malaposition, plaque prolapse and fibrous cap rupture according to stent design. Eur. J. Vasc. Endovasc. Surg. 2013, 45, 579–587. [CrossRef]

14. Okazaki, T.; Sakamoto, S.; Shinagawa, K.; Ichinose, N.; Ishii, D.; Matsushige, T.; Kiura, Y.; Kurisu, K. Detection of in-stent protrusion (ISP) by intravascular ultrasound during carotid stenting: Usefulness of stent-in-stent placement for ISP. Eur. Radiol. 2019, 29, 77–84. [CrossRef] [PubMed]

15. Nakagawa, I.; Kotsugi, M.; Park, H.S.; Furuta, T.; Sato, F.; Myochin, K.; Nishimura, F.; Yamada, S.; Motoyama, Y.; Nakase, H. Near-infrared spectroscopy carotid plaque characteristics and cerebral embolism in carotid artery stenting using first-generation stent. EuroIntervention 2021, 17, 599–606. [CrossRef]

16. Musialek, P.; Roubin, G.S. Double-Layer Carotid Stents: From the Clinical Need, through a Stent-in-Stent Strategy, to Effective Embolic Prevention Stent. J. Endovasc. Ther. 2019, 26, 572–577. [CrossRef]

17. Paraskevas, K.I.; Veith, F.J. Transcervical access, reversal of flow and mesh-covered stents: New options in the armamentarium of carotid artery stenting. World J. Cardiol. 2017, 9, 416–421. [CrossRef]

18. Musialek, P.; Hopkins, L.N.; Siddiqui, A. One swallow does not a summer make but many swallows do: Accumulating clinical evidence for nearly-eliminated peri-procedural and 30-day complications with meshcovered stents transforms the carotid revascularisation field. Adv. Inter. Ther. 2013, 13, 95–106. [CrossRef]

19. Schönholz, C.; Yamada, R.; Montgomery, W.; Brothers, T.; Guimaraes, M. First-in-man implantation of a new hybrid carotid stent to prevent peri-procedural neurological events during carotid artery stenting. J. Endovasc. Ther. 2014, 21, 601–604. [CrossRef]

20. Wissgott, C.; Schmidt, W.; Brandt, C.; Behrens, P.; Andresen, R. Preliminary Clinical Results and Mechanical Behavior of a New Double-Layer Carotid Stent. J. Endovasc. Ther. 2015, 22, 634–639. [CrossRef]

21. Wissgott, C.; Schmidt, W.; Brandt-Wunderlich, C.; Behrens, P.; Andresen, R. Clinical Results and Mechanical Properties of the Carotid CGUARD Double-Layered Embolic Prevention Stent. J. Endovasc. Ther. 2017, 24, 130–137. [CrossRef] [PubMed]

22. Musialek, P.; Mazurek, A.; Trystula, M.; Borrattynska, A.; Lesniak-Sobelga, A.; Urbanczyk, M.; Banys, R.P.; Brzychczy, A.; Zajdel, W.; Partyka, L.; et al. Novel PARADIGM in carotid revascularisation: Prospective evaluation of All-comer pErcutaneous cArOtidD revascularisation in symptomatic and Increased-risk asymptomatic carotid artery stenosis using CGuard™ MicroNet-covered embolic prevention stent system. EuroIntervention 2016, 12, e658–e670. [CrossRef] [PubMed]

23. Schofer, J.; Musialek, P.; Bijuklic, K.; Kolvenbach, R.; Trystula, M.; Siudak, Z.; Sievert, H. A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent the CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet). JACC Cardiovasc. Interv. 2015, 8, 1229–1234. [CrossRef] [PubMed]

24. Ruffino, M.A.; Faletti, R.; Bergamasco, L.; Fonio, P.; Righi, D. Incidence of New Ischaemic Brain Lesions After Carotid Artery Stenting versus endarterectomy in high-risk patients. N. Engl. J. Med. 2004, 351, 1493–1501. [CrossRef]

25. Arhuidese, I.J.; Rizwan, M.; Nejim, B.; Malas, M. Outcomes of Primary and Secondary Carotid Artery Stenting. Stroke 2017, 48, 3086–3092. [CrossRef] [PubMed]
32. Aronow, H.D.; Gray, W.A.; Ramee, S.R.; Mishkel, G.J.; Schreiber, T.J.; Wang, H. Predictors of neurological events associated with carotid artery stenting in high-surgical-risk patients: Insights from the Cordis Carotid Stent Collaborative. Circ Cardiovasc. Interv. 2010, 3, 577–584. [CrossRef]

33. Bibl, D.; Lampl, C.; Biberhofer, I.; Kerschner, K.; Kyppta, A.; Bergmann, J.; Kandilstorfer, A.; Roper, C.; Yazdi, K.; Engleder, C.; et al. Internal carotid artery stent placement without emboli protection: Results and long-term outcome. Neurology 2005, 65, 132–134. [CrossRef]

34. Capoccia, L.; Sirignano, P.; Mansour, W.; d’Adamo, A.; Sbarigia, E.; Mariani, P.; di Biasi, C.; Speziale, F. Peri-procedural brain lesions prevention in CAS (3PCSAS): Randomized trial comparing CGuard™ stent vs. Wallstent™. Int. J. Cardiol. 2019, 279, 148–153. [CrossRef]

35. De Haro, J.; Michel, I.; Bleda, S.; Cafibiano, C.; Acin, F. Carotid Stenting in Patients with High Risk Versus Standard Risk for Open Carotid Endarterectomy (REAL-1 Trial). Am. J. Cardiol. 2017, 120, 322–326. [CrossRef]

36. Diamond, J.; Madhavan, M.V.; Sabik, J.F.; Serruys, P.W.; Kappelein, A.P.; Leon, M.B.; Taggart, D.P.; Berland, J.; Morice, M.; Gersh, B.J.; et al. Left Main Percutaneous Coronary Intervention Versus Coronary Bypass Grafting in Patients with Prior Cerebrovascular Disease: Results from the EXCEL Trial. JACC Cardiovasc. Interv. 2018, 11, 2441–2450. [CrossRef]

37. Ecker, R.D.; Lau, T.; Levy, E.L.; Hopkins, L.N. Thirty-day morbidity and mortality rates for carotid artery intervention by surgeons who perform both carotid endarterectomy and carotid artery angioplasty and stent placement. J. Neurosurg. 2007, 106, 217–221. [CrossRef]

38. Eckstein, H.-H.; Ringleb, P.; Allenberg, J.-R.; Berger, J.; Fraedrich, G.; Hacke, W.; Hennerici, M.; Stingele, R.; Fiehler, J.; Zeumer, H.; et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) Study to treat symptomatic stenoses at 2 years: A multinational, prospective, randomized trial. Lancet Neurol. 2008, 7, 893–902. [CrossRef]

39. Featherstone, R.L.; Dobson, J.; Ederle, J.; Doig, D.; Bonati, L.H.; Morris, S.; Patel, N.; Brown, M.M. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): A randomised controlled trial with cost-effectiveness analysis. Health Technol. Assess. 2016, 20, 1–94. [CrossRef]

40. Gandini, R.; Del Giudice, C.; Da Ros, V.; Sallustio, F.; Altobelli, S.; D’Onofrio, A.; Abrignani, S.; Vasili, E.; Stanzione, P.; Simonetti, G. Long-term Results of Drug-Eluting Angioplasty for Treatment of Refractory Recurrent Carotid In-Stent Restenosis. J. Endovasc. Ther. 2014, 21, 671–677. [CrossRef]

41. González, A.; Gil-Peralta, A.; Mayol, A.; González-Marcos, J.; Moniche, F.; Aguilar, M.; Gutierrez, I. Internal Carotid Artery Stenting in Patients with Near Occlusion: 30-Day and Long-Term Outcome. Am. J. Neuroradiol. 2010, 32, 252–258. [CrossRef]

42. Goode, S.D.; Cleveland, T.J.; Gaines, P.A. United Kingdom carotid artery stent registry: Short- and long-term outcomes. Cardiovasc. Intervent. Radiol. 2013, 36, 1221–1231. [CrossRef]

43. Gory, B.; Piotin, M.; Haussen, D.C.; Steglich-Arnholm, H.; Holtmannspötter, M.; Labreuche, J.; Taschner, C.; Eiden, S.; Nogueira, R.G.; Papanagiotou, P.; et al. Thrombectomy in Acute Stroke with Tandem Occlusions From Dissection Versus Atherosclerotic Cause. Stroke 2017, 48, 3145–3148. [CrossRef]

44. Heck, D. Thirty day results of 227 consecutive carotid stent procedures performed in carotid stenting clinical trials. J. NeuroInterv. Surg. 2009, 1, 154–158. [CrossRef]

45. Higashida, R.T.; Popma, J.J.; Apprzzese, P.; Zimetbaum, P. MAVerIC I and II Investigators. Evaluation of the medtronic exponent Stent-Protected Angioplasty System (MnPAS) in the treatment of carotid stenosis: Combined results from the MAVerIC (Medtronic AVE Self-expanding CaRotid Stent System with distal protection in the treatment of carotid stenosis) I and MAVerIC II trials. Stroke 2010, 41, 102–109. [CrossRef]

46. Hill, M.; Morris, W.; Soulez, G.; Nevelsteen, A.; Maleux, G.; Rogers, C.; Hauptmann, K.; Bonafé, A.; Beyar, R.; Gruberg, L.; et al. Multicenter Evaluation of a Self-Expanding Carotid Stent System with Distal Protection in the Treatment of Carotid Stenosis. Am. J. Neuroradiol. 2006, 27, 759–765. [CrossRef]

47. Hopf-Jensen, S.; Marques, L.; Preiß, M.; Müller-Hülsbeck, S. Lesion-Related Carotid Angioplasty and Stenting with Closed-Cell Design without Embolic Protection Devices in High-Risk Elderly Patients-Can This Concept Work Out? A Single Center Experience Focusing on Stent Design. Int. J. Angiol. 2014, 23, 263–270. [CrossRef]

48. Howie, B.A.; Witek, A.M.; Hussain, M.S.; Bain, M.D.; Toth, G. Carotid Endarterectomy and Carotid Artery Stenting in aPredominantly Symptomatic Real-World Patient Population. World Neurosurg. 2019, 127, e722–e726. [CrossRef]

49. Huang, H.; Chen, K.; Guo, T.; Zhang, Y.; Qu, W.; Zhou, Z.; Liu, G.; Chen, L. Treatment with carotid angioplasty stent placement for post-stroke depression compared to antidepressants. Neurosciences 2012, 17, 53–56.

50. Itami, H.; Tokunaga, K.; Okuma, Y.; Hishikawa, T.; Sugiu, K.; Ida, K.; Date, I. Novel 3D-CT evaluation of carotid stent volume: Greater chronological expansion of stents in patients with vulnerable plaques. Neuroradiology 2013, 55, 1153–1160. [CrossRef]

51. Ito, K.; Kai, Y.; Hyodo, A.; Ishiuchi, S. Long-Term Outcome of Angioplasty or Stent Placement for Stenosis of the Cavernous or Petrous Portion of the Internal Carotid Artery. Neurol. Med. -Chir. 2011, 51, 813–818. [CrossRef]

52. Jones, M.R.; Howard, G.; Roubin, G.S.; Blackshear, J.L.; Cohen, D.J.; Cutlip, D.E.; Leimgruber, P.P.; Rhodes, D.; Prineas, R.J.; Glasser, S.P.; et al. Periprocedural Stroke and Myocardial Infarction as Risks for Long-Term Mortality in CREST. Circ. Cardiovasc. Qual. Outcomes 2018, 11, e004663. [CrossRef]

53. Jongen, L.M.; Hendrikse, J.; Waaier, A.; van der Worp, H.B.; Leijdekkers, V.J.; Lo, R.T.; Mali, W.P.T.M.; Prokop, M. Frequency and consequences of early in-stent lesions after carotid stent stent placement. J. Vasc. Interv. Radiol. 2009, 20, 573–579. [CrossRef]
96. Oteros, R.; Jimenez-Gomez, E.; Bravo-Rodriguez, F.; Ochoa, J.; Guerrero, R.; Delgado, F. Unprotected Carotid Artery Stenting in Symptomatic Patients with High-Grade Stenosis: Results and Long-Term Follow-Up in a Single-Center Experience. *Am. J. Neuroradiol.* 2012, 33, 1285–1291. [CrossRef]

97. Ouriel, K.; Wholey, M.H.; Fayad, P.; Katzen, B.T.; Whitlow, P.; Frentzkos, M.; Kuntz, R.E.; Wechsler, L.; Hopkins, N.; Satler, L.; et al. Feasibility Trial of Carotid Stenting with and Without an Embolus Protection Device. *J. Endovasc. Ther.* 2005, 12, 525–537. [CrossRef]

98. Paukovits, T.M.; Haász, J.; Molnár, A.; Széberin, Z.; Nemes, B.; Varga, D.; Hüttl, K.; Bérczi, V. Transfemoral endovascular treatment of proximal common carotid artery lesions: a single-center experience on 153 lesions. *J. Vasc. Surg.* 2008, 48, 80–87. [CrossRef]

99. Qureshi, A.I.; Kirmari, J.F.; Divani, A.A.; Hobson, R.W. Carotid Angioplasty with or without Stent Placement versus Carotid Endarterectomy for Treatment of Carotid Stenosis: A Meta-analysis. *Neurosurgery* 2005, 56, 1171–1181. [CrossRef]

100. Raabe, R.D.; Burr, R.B.; Short, R. One-year Cognitive Outcomes Associated with Carotid Artery Stent Placement. *J. Vasc. Interv. Radiol.* 2010, 21, 983–988. [CrossRef]

101. Randall, M.S.; McKevitt, F.M.; Kumar, S.; Cleveland, T.J.; Endean, K.; Venables, G.S.; Gaines, P.A. Long-Term Results of Carotid Artery Stents to Manage Symptomatic Carotid Artery Stenosis and Factors That Affect Outcome. *Circ. Cardiovasc. Interv.* 2010, 3, 50–56. [CrossRef][PubMed]

102. Schermerhorn, M.L.; Liang, P.; Eldrup-Jorgensen, J.; Cronenwett, J.L.; Nolan, B.W.; Kashyap, V.; Wang, G.J.; Motaganahalli, R.L.; Malas, M.B. Association of Transcarotid Artery Revascularization vs Transfemoral Carotid Artery Stenting with Stroke or Death Among Patients with Carotid Artery Stenosis. *JAMA* 2019, 322, 2313–2322. [CrossRef][PubMed]

103. Schreiber, T.L.; Strickman, N.; Davis, T.; Kumar, V.; Mishkel, G.; Foster, M.; Donohoe, D.; Britto, S.; Ansel, G. Carotid Artery Stenting with Emboli Protection Surveillance Study: Outcomes at 1 Year. *J. Am. Coll. Cardiol.* 2010, 56, 49–57. [CrossRef]

104. Setacci, C.; Chisci, E.; de Donato, G.; Sirignano, P.; Galzerano, G. Carotid artery stenting in a single center: Are six years of experience enough to achieve the standard of care? *Eur. J. Vasc. Endovasc. Surg.* 2007, 34, 655–662. [CrossRef]

105. SSYLVIA Study Investigators. Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA): Study results. *Stroke* 2004, 35, 1388–1392. [CrossRef]

106. Weinberg, I.; Beckman, J.A.; Shu, Y.; Jaff, M.R. Response by Weinberg et al to Letter Regarding Article, “Carotid Stent Fractures Are Not Associated with Adverse Events: Results From the ACT-1 Multicenter Randomized Trial (Carotid Angioplasty and Stenting Versus Endarterectomy in Asymptomatic Subjects Who Are at Standard Risk for Carotid Endarterectomy With Significant Extracranial Carotid Stenotic Disease)”. *Circulation* 2019, 137, 2676–2677. [CrossRef]

107. Yang, B.; Chen, W.; Yang, Y.; Lin, Y.; Duan, Y.; Li, J.; Wang, H.; Fu, F.; Zhuge, Q.; Chen, X. Short- and Long-Term Hemodynamic and Clinical Effects of Carotid Artery Stenting. *Am. J. Neuroradiol.* 2012, 33, 1170–1176. [CrossRef]

108. Zhu, Q.; Fang, S.; Wang, G.; Zhou, Z.; BIAN, S.; GUI, S.; YU, S.; WANG, F.; SHAN, L.; KANG, J. Clinical effects and safety review of self-expanding stent surgery for extracranial carotid artery stenosis treatment. *Genet. Mol. Res.* 2014, 13, 5128–5137. [CrossRef]

109. Liberati, A.; Altman, D.G.; Tetzlaff, J.; Mulrow, C.; Gotzsche, P.C.; Ioannidis, J.P.A.; Clarke, M.; Devereaux, P.J.; Kleijnen, J.; Moher, D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ* 2009, 339, b2700. [CrossRef]

110. Kohl, C.; McIntosh, E.J.; Unger, S.; Haddaway, N.R.; Kecke, S.; Schiemann, J.; Wilhelm, R. Online tools supporting the conduct and reporting of systematic reviews and systematic maps: A case study on CADIMA and review of existing tools. *Environ. Evid.* 2018, 7, 8. [CrossRef]

111. AbuRahma, A.F.; Abu-Halimah, S.; Bensenhaver, J.; Nanjundappa, A.; Stone, P.A.; Dean, L.S.; Keiffer, T.; Emmett, M.; Tarakji, M.; AbuRahma, Z. Primary carotid artery stenting versus carotid artery stenting for postcarotid endarterectomy stenosis. *J. Vasc. Surg.* 2009, 50, 1031–1039. [CrossRef]

112. Bayram, N.A.; Bozkurt, E.; Ayhan, H.; Gürkaş, E.; Orhan, G.; Ak, F.; Bilen, E.; Sari, C.; Akçay, M.; Durmaz, T.; et al. Early outcomes of carotid artery stenting. *Perfusion* 2012, 27, 146–149. [CrossRef][PubMed]

113. Akkan, K.; Ilgıt, E.; Oral, B.; Cindil, E.; Solak, E.P.; Onuc, F.; Geylan, D.E. Endovascular Treatment for Near Occlusion of the Internal Carotid Artery: 30-Day Outcome and Long-Term Follow-Up. *Clin. Neuroradiol.* 2018, 28, 245–252. [CrossRef][PubMed]

114. Alkins, R.; Matouk, C.C.; Cruz, J.P.; Marotta, T.; Montanera, W.; Spears, J. Carotid Artery Angioplasty and Stenting for Patients Less than 70 Years of Age. *Can. J. Neurol. Sci./J. Can. des Sci. Neurol.* 2009, 36, 245–252. [CrossRef] [PubMed]

115. Ansel, G.M.; Hopkins, L.N.; Jaff, M.R.; Rubino, P.; Basheer, J.; Scheinert, D.; Mela, S.; Das, T.; Cremonesi, A.; Investigators for the ARMOUR Pivotal Trial. Safety and effectiveness of the INVATEC MO.MA proximal cerebral protection device during carotid artery stenting: Results from the ARMOUR pivotal trial. *Catheter. Cardiovasc. Interv.* 2010, 76, 1–8. [CrossRef][PubMed]

116. Arslan, S.; Kökli, E.; Yüksel, İ.O.; Çağırıcı, G.; Bayar, N.; Yılmaz, A.; Büyük Gömclü, Y.; Erol, B. Two-year results of carotid artery stenting. *Turk. Kardiyol. Dern. Ars.* 2018, 42, 429–434. [CrossRef]

117. Bergeron, P.; Roux, M.; Khanoyan, P.; Douillez, V.; Bras, J.; Gay, J. Long-term results of carotid artery stenting are competitive with surgery. *J. Vasc. Surg.* 2005, 41, 213–221. [CrossRef]

118. Biggs, N.G.; Rangarajan, S.; McClure, D.N. Has carotid artery stenting found its place? A 10-year regional centre perspective. *ANZ J. Surg.* 2014, 84, 179–183. [CrossRef]

119. Bijuklic, K.; Wandler, A.; Hazizzi, F.; Schofer, J. The PROFI Study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting): A Prospective Randomized Trial. *J. Am. Coll. Cardiol.* 2012, 59, 1383–1389. [CrossRef]
120. Bosiers, M.; De Donato, G.; Deloose, K.; Verbist, J.; Peeters, P.; Castriota, F.; Cremonesi, A.; Setacci, C. Does free cell area influence the outcome in carotid artery stenting? *Eur. J. Vasc. Endovasc. Surg.* 2007, 33, 135–141. [CrossRef]

121. Bosiers, M.; Deloose, K.; Torsello, G.; Scheinert, D.; Mathias, K.; Langhoff, R.; Mudra, H.; Diaz-Cartelle, J. Carotid Stenting with Distal Protection in High-Surgical-Risk Patients: One-Year Results of the ASTI Trial. *Cardiovasc. Inter. Radiol.* 2014, 38, 295–303. [CrossRef]

122. Bosiers, M.; Scheinert, D.; Mathias, K.; Langhoff, R.; Mudra, H.; Diaz-Cartelle, J. Carotid Stenting with Distal Protection in High-Surgical-Risk Patients: One-Year Results of the ASTI Trial. *Cardiovasc. Inter. Radiol.* 2014, 38, 295–303. [CrossRef]

123. Brewster, L.P.; Beaullieu, R.; Corriere, M.A.; Veeraraswamy, R.; Niazi, K.A.; Robertson, G.; Dodson, T.E.; Kasirajan, K. Carotid revascularization outcomes comparing distal filters, flow reversal, and endarterectomy. *J. Vasc. Surg.* 2011, 54, 1000–1005. [CrossRef] [PubMed]

124. Brott, T.G.; Hobson, R.W.; Howard, G.; Roubin, G.S.; Clark, W.M.; Brooks, W.; Mackey, A.; Hill, M.D.; Leimgruber, P.P.; Sheffet, A.J.; et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N. Engl. J. Med.* 2010, 363, 11–23. [CrossRef] [PubMed]

125. Buszman, P.P.; Szymański, R.; Dębowski, M.; Milewski, K.; Krol, M.; Nowakowski, P.; Kiesz, R.S.; Radvany, M.G.; Wierneck, S.; Wiernek, B.; et al. Long-term results of cephalad arteries percutaneous transluminal angioplasty with stent implantation (The CAPTAS registry). *Catheter. Cardiovasc. Inter.* 2012, 79, 532–540. [CrossRef] [PubMed]

126. Casana, R.; Tolva, V.; Odero, A.; Malloggi, C.; Paolucci, A.; Triulzi, F.; Silani, V. Safety and Efficacy of the New Micromesh-Covered Stent CGuard in Patients Undergoing Carotid Artery Stenting: Early Experience from a Single Centre. *Eur. J. Vasc. Endovasc. Surg.* 2017, 54, 681–687. [CrossRef] [PubMed]

127. De Castro-Afonso, L.H.; Nakiri, G.S.; Monsignore, L.M.; dos Santos, D.; Camilo, M.R.; Dias, F.A.; Cougo-Pinto, P.T.; Barreira, C.M.A.; Alessio-Alves, F.F.; Fábio, S.R.C.; et al. Outcomes of carotid artery stenting at a high-volume Brazilian interventional neuroradiology center. *Clinics* 2015, 70, 180–184. [CrossRef]

128. Chung, C.; Cayne, N.S.; Adelman, M.A.; Riles, T.S.; Lamparello, P.; Han, D.; Marin, M.L.; Faries, P.L.; Lamparello, P. Improved Hemodynamic Outcomes with Glycopyrrolate Over Atropine in Carotid Angioplasty and Stenting. *Perspect. Vasc. Surg. Endovasc. Ther.* 2010, 22, 164–170. [CrossRef]

129. Chung, G.; Jeon, J.; Kwak, H.; Hwang, S. Associations between Cerebral Embolism and Carotid Intraplaque Hemorrhage during Protected Carotid Artery Stenting. *Am. J. Neuroradiol.* 2015, 37, 686–691. [CrossRef]

130. Cieri, E.; De Rango, P.; Maccaroni, M.R.; Spaccatini, A.; Caso, V.; Cao, P. Is haemodynamic depression during carotid stenting a predictor of peri-procedural complications? *Eur. J. Vasc. Endovasc. Surg.* 2008, 35, 399–404. [CrossRef]

131. Clair, D.G.; Hopkins, L.N.; Mehta, M.; Kasirajan, K.; Schermerhorn, M.; Schönholz, C.; Kwolek, C.J.; Eskandari, M.K.; Powell, R.J.; Ansel, G.M.; et al. Neuroprotection during carotid artery stenting using the GORE flow reversal system: 30-day outcomes in the EMPIRE Clinical Study. *Catheter. Cardiovasc. Inter.* 2010, 77, 420–429. [CrossRef] [PubMed]

132. Chung, G.; Jeong, J.; Kwak, H.; Hwang, S. Associations between Cerebral Embolism and Carotid Intraplaque Hemorrhage during Protected Carotid Artery Stenting. *Am. J. Neuroradiol.* 2015, 37, 686–691. [CrossRef]

133. Cieri, E.; De Rango, P.; Maccaroni, M.R.; Spaccatini, A.; Caso, V.; Cao, P. Is haemodynamic depression during carotid stenting a predictor of peri-procedural complications? *Eur. J. Vasc. Endovasc. Surg.* 2008, 35, 399–404. [CrossRef]

134. Eskandari, M.K.; Usman, A.A.; García-Toca, M.; Matsumura, J.S.; Kibbe, M.R.; Morasch, M.D.; Rodriguez, H.E.; Pearce, W.H. Eight-year institutional review of carotid artery stenting. *J. Vasc. Surg.* 2010, 51, 1145–1151. [CrossRef] [PubMed]

135. Faggioli, G.; Pini, R.; Rapesti, C.; Mauro, R.; Freyrie, A.; Gargiulo, M.; Reggiani, L.B.; Stella, A. Carotid Revascularization in Patients with Ongoing Oral Anticoagulant Therapy: The Advantages of Stent Placement. *J. Vasc. Inter. Radiol.* 2013, 24, 370–377. [CrossRef]

136. Faggioli, G.; Pini, R.; Rapesti, C.; Mauro, R.; Freyrie, A.; Gargiulo, M.; Reggiani, L.B.; Stella, A. Carotid Revascularization in Patients with Ongoing Oral Anticoagulant Therapy: The Advantages of Stent Placement. *J. Vasc. Inter. Radiol.* 2013, 24, 370–377. [CrossRef]

137. Faggioli, G.; Pini, R.; Rapesti, C.; Mauro, R.; Freyrie, A.; Gargiulo, M.; Reggiani, L.B.; Stella, A. Carotid Revascularization in Patients with Ongoing Oral Anticoagulant Therapy: The Advantages of Stent Placement. *J. Vasc. Inter. Radiol.* 2013, 24, 370–377. [CrossRef]

138. Faggioli, G.; Pini, R.; Rapesti, C.; Mauro, R.; Freyrie, A.; Gargiulo, M.; Reggiani, L.B.; Stella, A. Carotid Revascularization in Patients with Ongoing Oral Anticoagulant Therapy: The Advantages of Stent Placement. *J. Vasc. Inter. Radiol.* 2013, 24, 370–377. [CrossRef]

139. Goldstein, L.J.; Khan, H.U.; Sambol, E.B.; Kent, K.C.; Faries, P.L.; Vouyouka, A.G. Carotid artery stenting is safe and associated with comparable outcomes in men and women. *J. Vasc. Surg.* 2009, 49, 315–324. [CrossRef]

140. Gray, W.A.; Rosenfield, K.A.; Jaff, M.R.; Chaturvedi, S.; Verta, P.; Jaff, M.R.; Chaturvedi, S.; Verta, P.; Jaff, M.R.; Chaturvedi, S.; Verta, P. Influence of Site and Operator Characteristics on Carotid Artery Stent Outcomes: Analysis of the CAPTURE 2 (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events) Clinical Study. *JACC Cardiovasc. Inter.* 2011, 4, 235–246. [CrossRef]

141. Gray, W.A.; Yadav, J.S.; Verta, P.; Scicli, A.; Fairman, R.; Wholey, M.; Hopkins, L.N.; Atkinson, R.; Raabe, R.; Barnwell, S.; et al. The CAPTURE registry: Predictors of outcomes in carotid artery stenting with embolic protection for high surgical risk patients in the early post-approval setting. *Catheter. Cardiovasc. Inter.* 2007, 70, 1025–1033. [CrossRef] [PubMed]

142. Gruberg, L.; Jeremias, A.; Rundback, J.H.; Anderson, H.V.; Spertus, J.A.; Kennedy, K.F.; Rosenfield, K.A. Impact of Glomerular filtration rate on clinical outcomes after carotid artery revascularization in 11,832 patients from the CARE registry®. *Catheter. Cardiovasc. Inter.* 2014, 84, 246–254. [CrossRef] [PubMed]
187. Rabe, K.; Sugita, J.; Gödel, H.; Sievert, H. Flow-Reversal Device for Cerebral Protection During Carotid Artery Stenting-Acute and Long-Term Results. J. Interv. Cardiol. 2006, 19, 55–62. [CrossRef]

188. Rhee-Moore, S.; Derubertis, B.G.; Lam, R.C.; Hynecek, R.L.; Lee, L.; McKinsey, J.F.; Morrissey, N.J.; Karwowski, J.; Mureebe, I.; Kent, K.C.; et al. Periprocedural Complication Rates Are Equivalent between Symptomatic and Asymptomatic Patients Undergoing Carotid Angioplasty and Stenting. Ann. Vasc. Surg. 2008, 22, 233–237. [CrossRef]

189. Roffi, M.; Greutmann, M.; Eberli, F.R.; Rainoni, L.; Lüscher, T.F.; Amann-Vesti, B.; Schwarz, U. Starting a carotid artery stenting program is safe. Catheter. Cardiovasc. Interv. 2008, 71, 469–473. [CrossRef]

190. Safian, R.D.; Bresnahan, J.F.; Jaff, M.R.; Foster, M.; Bacharach, J.M.; Maini, B.; Turco, M.; Myla, S.; Eles, G.; Ansel, G.M. Protected Carotid Stenting in High-Risk Patients with Severe Carotid Artery Stenosis. J. Am. Coll. Cardiol. 2006, 47, 2384–2389. [CrossRef]

191. Scheinert, D.; Reimers, B.; Cremonesi, A.; Schmidt, A.; Sievert, H.; Rohde, S.; Schofer, J.; Mudra, H.G.; Bosiers, M.; et al. Protected Carotid Stenting in High-Risk Patients: Results of the SpideRX Arm of the Carotid Revascularization with ev3 Arterial Technology Evolution Trial. J. Interv. Cardiol. 2010, 23, 491–498. [CrossRef]

192. Sahin, M.; Acar, G.; Özkan, B.; Alıcıı, G.; Yazıcıoglu, M.V.; Bulut, M.; Kalkan, M.E.; Demir, S.; Acar, R.D.; Boztosun, B. Comparison of short-term outcomes after carotid artery stenting according to different stent designs. Adv. Interv. Cardiol. 2013, 2, 121–125. [CrossRef]

193. Sahin, M.; Yazıcıoglu, M.V.; Acar, G.; Demir, S.; Kalkan, M.E.; Özkan, B.; Alici, G.; Akgun, T.; Akcakoyun, M.; Boztosun, B. Safety of balloon pre-dilatation in the treatment of severe carotid artery stenosis. Eur. Rev. Med Pharmacol. Sci. 2013, 17, 788–793.

194. Sakamoto, S.; Kiura, Y.; Shinagawa, K.; Ichinose, N.; Shibukawa, M.; Orita, Y.; Myla, S.; Eles, G.; Ansel, G.M. Protection of carotid stenting in high-risk patients: The EVAR2 study. J. Vasc. Surg. 2008, 48, 1209–1218. [PubMed]

195. Saw, J.; Bajzer, C.; Casserly, I.P.; Exaire, E.; Haery, C.; Sachar, R.; Lee, D.; Abou-Chebl, A.; Yadav, J.; Joye, J.; Myla, S.; Kassab, E.; Mann, J.T.; et al. The EVAR2 study: A single-center experience with up to 8 years’ follow-up. Eur. J. Vasc. Endovasc. Surg. 2010, 40, 369–378. [CrossRef]

196. Scheinert, D.; Reimers, B.; Cremonesi, A.; Schmidt, A.; Sievert, H.; Rohde, S.; Schofer, J.; Mudra, H.G.; Bosiers, M.; Zeller, T.; et al. Independent Modular Filter for Embolic Protection in Carotid Stenting. Circ. Cardiovasc. Interv. 2017, 10, 004244. [CrossRef]

197. Setacci, C.; de Donato, G.; Chisci, E.; Stella, A.; Faggioni, G.; Reimers, B.; Cernetti, C.; Quijada, M.L.; Cappi, B.; Sangiorgi, G. Deferred Urgency Carotid Artery Stenting in Symptomatic Patients: Clinical Lessons and Biomarker Patterns from a Prospective Registry. Eur. J. Vasc. Endovasc. Surg. 2008, 35, 644–651. [CrossRef]

198. Shen, S.; Jiang, X.; Dong, H.; Peng, M.; Wang, Z.; Che, W.; Zou, Y.; Yang, Y. Effect of aortic arch type on technical indicators in patients undergoing carotid artery stenting. J. Int. Med Res. 2018, 47, 682–688. [CrossRef]

199. Shin, S.H.; Stout, C.L.; Richardson, A.I.; DeMasi, R.J.; Shah, R.M.; Panneton, J.M. Carotid angioplasty and stenting in anatomically high-risk patients: Safe and durable except for radiation-induced stenosis. J. Vasc. Surg. 2009, 50, 762–767. [CrossRef]

200. Simonetti, G.; Gandini, R.; Versaci, F.; Pampena, E.; Fabiano, S.; Stefanini, M.; Spinelli, A.; Reale, C.A.; Di Primio, M.; Gaspari, E. Carotid artery stenting: A single-centre experience with up to 8 years' follow-up. Eur. Radiol. 2008, 19, 982–989. [CrossRef]

201. Sirignano, P.; Stabile, E.; Mansour, W.; Speziale, F. One-month results from a prospective experience on CAS using C-GUARD stent system: The IRONGUARD-2 study. Eur. Heart J. 2020, 41, 2170–2177. [CrossRef]

202. Spacek, M.; Zimolova, P.; Veselka, J. Carotid Artery Stenting Without Post-Dilation. J. Interv. Cardiol. 2011, 25, 190–196. [CrossRef]

203. Speziale, F.; Capoccia, L.; Sirignano, P.; Mansour, W.; Pranteda, C.; Casana, R.; Setacci, C.; Accrocca, F.; Alberti, D.; de Donato, G.; et al. Thirty-day results from prospective multi-specialty evaluation of carotid artery stenting using the CGuard MicroNet-covered Embolic Protection System in real-world multicentre clinical practice: The IRON-Guard study. EuroIntervention 2018, 13, 1714–1720. [CrossRef]

204. Stabile, E.; Salemmie, L.; Sorropago, G.; Tesorio, T.; Nammas, W.; Miranda, M.; Popuso, G.; Cioppa, A.; Ambrosini, V.; Cota, L.; et al. Proximal Endovascular Occlusion for Carotid Artery Stenting: Results from a Prospective Registry of 1,300 Patients. J. Am. Coll. Cardiol. 2010, 55, 1661–1667. [PubMed]

205. Stanziale, S.F.; Marone, L.K.; Boules, T.N.; Brimmeier, J.A.; Hill, K.; Makaroun, M.S.; Wholey, M.H. Carotid artery stenting in octogenarians is associated with increased adverse outcomes. J. Vasc. Surg. 2006, 43, 297–304. [CrossRef]

206. Tadros, R.O.; Spyris, C.T.; Vouyouka, A.G.; Chung, C.; Krishnan, P.; Arnold, M.W.; Marin, M.L.; Faries, P.L. Comparing the embolic potential of open and closed cell stents during carotid angioplasty and stenting. J. Vasc. Surg. 2012, 56, 89–95. [CrossRef]

207. Takigawa, T.; Matsumaru, Y.; Hayakawa, M.; Nemoto, S.; Matsumura, A. Cilostazol reduces restenosis after carotid artery stenting. J. Vasc. Surg. 2010, 51, 51–56. [CrossRef]

208. Tang, G.L.; Matsumura, J.S.; Morasch, M.D.; Pearce, W.H.; Nguyen, A.; Amaranto, D.; Eskandari, M.K. Carotid angioplasty and stenting vs carotid endarterectomy for treatment of asymptomatic disease: Single-center experience. Arch. Surg. 2008, 143, 653. [CrossRef]

209. Tas, M.H.; Simsek, Z.; Colak, A.; Koza, Y.; Demir, P.; Demir, R.; Kaya, U.; Tanboga, I.H.; Gundogdu, F.; Sevimli, S. Comparison of Carotid Artery Stenting and Carotid Endarterectomy in Patients with Symptomatic Carotid Artery Stenosis: A Single Center Study. Adv. Ther. 2013, 30, 845–853. [CrossRef]

210. Tatli, E.; Tokatli, A.; Vatan, M.B.; Agac, M.T.; Gunduz, H.; Akdemir, R.; Kilic, H. Comparison of closed-cell and hybrid-cell stent designs in carotid artery stenting. Clin. and procedural outcomes. Adv. Interv. Cardiol. 2017, 2, 135–141. [CrossRef]
211. Ullery, B.W.; Orlova, K.; Shang, E.K.; Jackson, B.M.; Wang, G.J.; Fairman, R.M.; Woo, E.Y. Results of carotid angioplasty and stenting are equivalent for critical versus high-grade lesions in patients deemed high risk for carotid endarterectomy. J. Surg. Res. 2013, 185, 21–26. [CrossRef]

212. Van der Heyden, J.; Wolters, F.J.; Garin, N.; Blant, S.A.; Inglin, M.; Bal, E.T.; Suttrop, J.M. The role of embolic protection devices during carotid stenting prior to cardiac surgery in asymptomatic patients: Empty filters? Catheter. Cardiovasc. Interv. 2012, 80, 112–119. [CrossRef]

213. Veselka, J.; Zimolová, P.; Martinkovičová, L.; Tomášov, P.; Hájek, P.; Malý, J.; Zemanek, D.; Tesař, D.; Tomášov, P. Comparison of mid-term outcomes of carotid artery stenting for moderate versus critical stenosis. Arch. Med. Sci. 2012, 8, 75–80. [CrossRef]

214. Yoshida, S.; Bensley, R.P.; Glaser, J.D.; Nabzdyk, C.S.; Hamdan, A.D.; Wyers, M.C.; Chaikof, E.L.; Schermerhorn, M.L. The current...

215. Wieker, C.M.; Demirel, S.; Attigah, N.; Hakimi, M.; Förste, T.; Leschke, M.; et al. Carotid Artery Stenting in Clinical Practice: Does Sex Matter? Results From the Carotid Artery Stenting Registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK). Clin. Cardiol. 2013, 35, 111–118. [CrossRef] [PubMed]

216. Wissgott, C.; Brandt-Wunderlich, C.; Kopetsch, C.; Schmidt, A.; et al. 1-Year Results from a Prospective Experience on CAS Using the CGuard Stent System: The IRONGUARD 2 Study. JACC 2011, 25, 796–804. [CrossRef] [PubMed]

217. Yoon, W.; Kim, S.K.; Park, M.; Chae, H.; Kang, H. Safety of Protected Carotid Artery Stenting in Patients with Severe Carotid... [CrossRef]

218. Yang, L.; Liu, J.; Qi, G.; Li, Y.; Liu, Y. The middle-term outcome of carotid endarterectomy and stenting for treatment of ischemic... [CrossRef]

219. Yan, D.; Tang, X.; Shi, Z.; Wang, L.; Lin, C.; Guo, D.; Fu, W. Perioperative and Follow-up Results of Carotid Artery Stenting and Carotid Endarterectomy in Patients with Carotid Near-Occlusion. Ann. Vasc. Surg. 2019, 59, 21–27. [CrossRef]

220. Yen, M.H.; Lee, D.S.; Kapadia, S.; Sachar, R.; Bhatt, D.L.; Bajzer, C.T.; Yadav, J.S. Symptomatic patients have similar outcomes compared with asymptomatic patients after carotid artery stenting with emboli protection. Am. J. Cardiol. 2005, 95, 297–300. [CrossRef]

221. Yoon, W.; Kim, S.K.; Park, M.; Chae, H.; Hong, S.H. Safety of Protected Carotid Artery Stenting in Patients with Severe Carotid Artery Stenosis and Carotid Intraluminal Hemorrhage. Am. J. Neuroradiol. 2012, 33, 1027–1031. [CrossRef]

222. Yoshida, S.; Bensley, R.P.; Glaser, J.D.; Hamdan, A.D.; Wyers, M.C.; Chaikof, E.L.; et al. The current national criteria for carotid artery stenting overestimate its efficacy in patients who are symptomatic and at high risk. J. Vasc. Surg. 2013, 58, 120–127. [CrossRef]

223. Yoshida, S.; Yamaoka, K.; Nogami, M.; Kajikawa, T.; Suyama, H.; et al. Clinical trial of carotid artery stenting using dual-layer CASPER stent for carotid endarterectomy in patients with high and normal risk in the Japanese population. J. Neurointerv. Surg. 2021, 13, 524–529. [CrossRef]

224. Yokoishi, K.; Nogami, T.; Sugawara, Y.; et al. Comparison of Restenosis Risk in Single-Layer versus Dual-Layer Carotid Stents: A Duplex Ultrasound Evaluation. Cardiovasc. Intervent. Radiol. 2022. ahead of print. [CrossRef]

225. Yokoishi, K.; Nogami, T.; Sugawara, Y.; et al. Randomized comparison of carotid artery stenting versus carotid endarterectomy. J. Endovasc. Ther. 2021, 28, 542–548. [CrossRef]

226. Yokoishi, K.; Nogami, T.; Sugawara, Y.; et al. 1-Year Results from a Prospective Experience on CAS Using CGuard Stent System: The IRONGUARD 2 Study. JACC Cardiovasc. Interv. 2020, 13, 2170–2177. [CrossRef]

227. Yokoishi, K.; Nogami, T.; Sugawara, Y.; et al. 1-Year Results from a Prospective Experience on CAS Using CGuard Stent System: The IRONGUARD 2 Study. JACC Cardiovasc. Interv. 2020, 13, 2170–2177. [CrossRef]

228. Yokoishi, K.; Nogami, T.; Sugawara, Y.; et al. 1-Year Results from a Prospective Experience on CAS Using CGuard Stent System: The IRONGUARD 2 Study. JACC Cardiovasc. Interv. 2020, 13, 2170–2177. [CrossRef]
233. Dakour-Aridi, H.; Mathlouthi, A.; Locham, S.; Goodney, P.; Schermerhorn, M.L.; Malas, M.B. Predictors of midterm high-grade restenosis after carotid revascularization in a multicenter national database. *J. Vasc. Surg.* **2020**, *71*, 1972–1981. [CrossRef]

234. Galyfos, G.C.; Tsoutsas, I.; Konstantopoulos, T.; Galanopoulos, G.; Sigala, F.; Filis, K.; Papavassiliou, V. Early and Late Outcomes after Transcarotid Revascularisation for Internal Carotid Artery Stenosis: A Systematic Review and Meta-Analysis. *Eur. J. Vasc. Endovasc. Surg.* **2021**, *61*, 725–738. [CrossRef]

235. Trystula, M.; Musialek, P. Transient flow reversal combined with sustained embolic prevention in transcervical revascularization of symptomatic and highly-emboligenic carotid stenoses for optimized endovascular lumen reconstruction and improved peri- and post-procedural outcomes. *Adv. Interv. Cardiol.* **2020**, *16*, 495–506.

236. Musialek, P.; Mazurek, A.; Kolvenbach, R.; Malinowski, K.; Brinkmann, C.; Sievert, H.; Schofer, J. 5-year Clinical and Ultrasound Outcomes in CARENET Prospective Multicenter Trial of CGuard MicroNET-Covered Carotid Stent (CARotid Embolic Prevention using MicroNET-Covered Stent System in Patients with Symptomatic and Asymptomatic Carotid Artery Stenosis). *JACC Cardiovasc. Interv.* **2022**, in press.

237. Texakalidis, P.; Giannopoulos, S.; Kokkinidis, D.G.; Lanzino, G. Effect of Open- vs Closed-Cell Stent Design on Periprocedural Outcomes and Restenosis After Carotid Artery Stenting: A Systematic Review and Comprehensive Meta-analysis. *J. Endovasc. Ther.* **2018**, *25*, 523–533. [CrossRef] [PubMed]

238. White, C.J.; Brott, T.G.; Gray, W.A.; Heck, D.; Jovin, T.; Lyden, S.P.; Metzger, D.C.; Rosenfield, K.; Roubin, G.; Sachar, R.; et al. Carotid Artery Stenting: JACC State-of-the-Art Review. *J. Am. Coll. Cardiol.* **2022**, *80*, 155–170. [CrossRef] [PubMed]