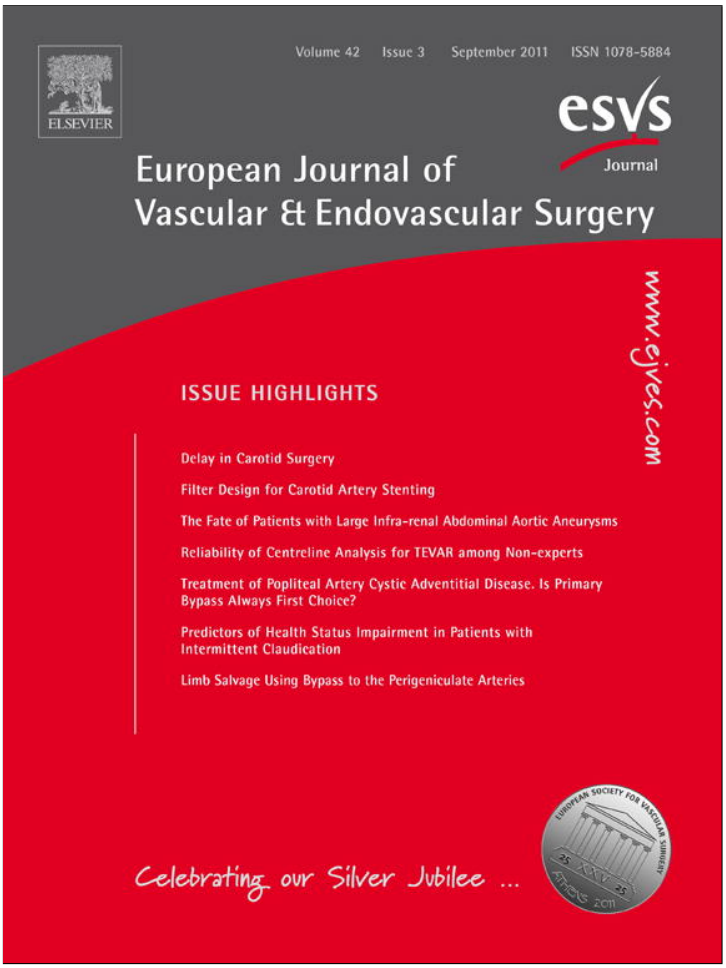

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The Association of Clinical Variables and Filter Design with Carotid Artery Stenting Thirty-day Outcome

G.M. Siewiorek [a], R.T. Krafty [b], M.H. Wholey [c], E.A. Finol [d,*]

[a] *Biomedical Engineering Department, Carnegie Mellon University, 1210 Hamburg Hall, 5000 Forbes Avenue, Pittsburgh, PA 15213, USA*
[b] *Department of Statistics, University of Pittsburgh, 2702 Cathedral of Learning, Pittsburgh, PA 15260, USA*
[c] *University of Pittsburgh Medical Center – Shadyside, 5230 Centre Avenue, Suite 603, Pittsburgh, PA 15232, USA*
[d] *Institute for Complex Engineered Systems, Biomedical Engineering Department and Department of Mechanical Engineering, 1205 Hamburg Hall, 5000 Forbes Avenue, Carnegie Mellon University, Pittsburgh, PA 15213, USA*

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Abstract *Objective:* Patient and device selection are important for the success of carotid artery stenting (CAS). We hypothesize that distal protection filter (DPF) design characteristics that minimize blood flow resistance and maximize capture efficiency are associated with the absence of transient ischemic attack (TIA), stroke and neurologic-related death after 30 days.
Methods: Records from 208 patients were reviewed retrospectively. Filter design characteristics were quantified previously in our laboratory. The association between risk factors and design characteristics with 30-day outcome was quantified using univariate analysis.
Results: The 30-day all-cause stroke and death rate was 8.7% (asymptomatic: 7.7%, symptomatic: 10.6%). Five DPFs were used in the study: Accunet (41.3%), Angioguard (33.2%), FilterWire (24%), Emboshield (1%), and Spider (.5%). Diabetes ($P = .04$) and prior carotid endarterectomy (CEA, $P = .03$) were associated with adverse outcome. Prior stroke ($P = .01$) and prior CEA ($P = .04$) were significant for peri-procedural stroke. Design characteristics such as capture efficiency were associated with favorable outcomes.
Conclusions: Patients with prior CEA or stroke are more likely to have unfavorable CAS outcomes after 30 days. Filters with high capture efficiency may yield the best clinical results. Analysis of the effect of design characteristics on CAS outcome should aid the design of future devices.

* Corresponding author. Institute for Complex Engineered Systems, Carnegie Mellon University, 1205 Hamburg Hall, 5000 Forbes Avenue, Pittsburgh, PA 15213, USA. Tel.: +1 412 268 1841; fax: +1 412 268 5229.
E-mail address: finole@cmu.edu (E.A. Finol).

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Introduction

The surgical (carotid endarterectomy [CEA]) and endovascular (carotid artery stenting [CAS]) treatments of carotid artery occlusive disease are perceived to be complementary procedures. Thus, patient selection is considered crucial to the success of either form of treatment. It is widely accepted that the use of cerebral protection devices (CPDs) is crucial to the success of CAS.[1] In particular, distal protection filters (DPFs) are widely used due to their ability of maintaining peri-procedural blood flow. The selection of stents and cerebral protection devices is also important for favorable outcome.[2]

Previous studies have examined the effect risk factors,[3–10] blood flow (measurements using hypotension[11] or hemodynamic instability[12]), lesion characteristics,[13] and plaque composition (determined by amount of debris trapped by the CPD,[14] by histology,[15] and by intravascular ultrasound[16]) have on CAS patient outcome. Few studies have incorporated device design characteristics in their analysis other than stent cell type.[2,17–21] Roffi,[22] Hart,[2] and Iyer[23] examined the effects of DPFs on peri-procedural flow impairment, concentricity of DPFs on 30-day patient outcomes, and type of CPD on 30-day patient outcomes, respectively. These studies classified DPFs based on eccentricity, but did not evaluate the specific design features, concluding that further analysis of device design characteristics is necessary.[2] Our laboratory has previously quantified key DPF design characteristics and studied their effect on filter capture efficiency and flow resistance using a bench-top testing apparatus.[24] We hypothesize that DPF design characteristics that minimize resistance to blood flow and maximize emboli capture efficiency will be negatively associated with adverse 30-day patient outcome. Therefore, the goal of this investigation is to quantify the association between clinical and DPF design characteristics, and assess their respective relationship to adverse CAS outcome (i.e., the occurrence of transient ischemic attack [TIA], stroke, or neurologic-related death) within 30 days of the procedure.

Methods

A retrospective review of medical records of CAS patients was pursued following approval of an Institutional Review Board protocol waivering HIPAA authorization by the local ethics committees. Patient information was de-identified to exclude the patient's name, social security number, address and telephone number, medical record number, or any other information that could be used to identify the patient. The records were stored electronically, and were locked and secured. The clinical and 30-day outcome data was recorded for 208 patients treated non-consecutively at University of Pittsburgh Medical Center (UPMC) — Shadyside campus between July 2000 and October 2006. All patients were treated by one interventionist (MHW). Patients included in the study underwent CAS protected with a DPF and had 30-day follow-up data available on their records, which included but was not limited to the occurrence of myocardial infarct (MI), TIA, stroke, or death due to any cause within 30 days of the procedure. Additional inclusion and exclusion criteria were based upon the specific trial in which each patient was enrolled, including SAPPHIRE,[25] ARCHeR,[26] BEACH,[27] CABERNET,[28] and CREST.[29] There was overlap in the inclusion and exclusion criteria among these trials. General inclusion criteria included age greater than 18 years, symptomatic stenosis greater than 50%, asymptomatic stenosis greater than 70% (CREST) or 80%, and at least one high-risk criterion (high-risk trials). Typical exclusion criteria included total ipsilateral occlusion, recent stroke, and known source of cardiac emboli.

Baseline characteristics were collected for each patient, including age, sex, cardiovascular risk factors, history of cardiovascular disease, and medical history. Please refer to Table 1 for a complete list of variables examined in the study. DPF design characteristics, including capture efficiency, vascular resistance, porosity, pore density, eccentricity, and wall apposition, were measured previously.[24,30,31] The capture efficiency of each DPF was measured in a bench-top flow apparatus where 5 mg of microspheres were injected into the system, simulating plaque embolization.[30] The ideal capture efficiency was 100%. Vascular resistance was calculated as the ratio of the pressure gradient across the distal protection filter to the flow rate in the flow model.[30] Porosity and pore density were calculated using images captured by a CCD camera mounted on a microscope.[24] Porosity was defined as the ratio of porous surface area to total surface area, while pore density was defined as the ratio of number of pores to total surface area. Wall apposition was quantified using photographs of the DPF in the coronal plane; the ideal wall apposition was 0%, where there are no gaps between the DPF and the vessel wall.[31]

Generally, the CAS procedures followed a similar protocol: patients were treated with aspirin prior to the procedure and continued indefinitely. They received clopidogrel 24 h before the procedure and for 3—4 months following the procedure. Nearly all patients received bivalirudin unless they arrived to the angiography suite on unfractionated heparin, in which case, heparin was the anticoagulant, maintaining an activated partial-thromboplastin time of 250—300 s. Access was gained through the common femoral artery. The lesion was crossed with the DPF guidewire and expanded. After the stent was deployed, it was post-dilated and the filter collapsed and removed.

Statistical Analysis

Univariate analysis was used to quantify the association between each binary clinical variable and each individual outcome (TIA, stroke, neurologic-related death, after 30-days) and composite adverse event outcome (occurrence of any individual outcome) at a significance level of $\alpha = .05$ using SAS v9.2 (SAS Institute Inc., Cary, NC). The p-value, odds ratio (OR), and 95% confidence interval (CI) were reported for each clinical variable. Subgroup analysis of symptomatic status and octogenarians were also conducted. Significant variables found in univariate analysis were used for multivariate analysis, although, in general, the consensus is that 10 subjects are required for each covariate; thus, at most 2 covariates could be examined simultaneously.[32] After variable selection, the importance of each variable was assessed by a Wald statistic value greater than 2, which is approximately an $\alpha = .05$

Table 1 Patient characteristics and their *p*-value, odds ratio, and 95% confidence interval.

Characteristic	Number (Percentage)	TIA *p-value* *OR* (95% CI)	Stroke *p-value* *OR* (95% CI)	Death *p-value* *OR* (95% CI)	Adverse Event *p-value* *OR* (95% CI)
Age > 80 years	33 (16.1)	.96 n/a	.85 1.2 (.2–5.7)	.09 5.5 (.7–40.4)	.61 .7 (.1–3.1)
Male	137 (66.8)	.58 .7 (.1–3.0)	.38 .6 (.2–2.0)	.96 n/a	.47 .7 (.2–1.9)
Diabetes mellitus	63 (30.7)	.14 3.1 (.7–14.5)	.28 2.0 (.6–6.7)	.41 2.3 (.3–16.7)	.04 2.8 (1.0–7.6)
History of dyslipidemia	143 (69.8)	.92 1.1 (.2–5.8)	.65 .7 (.2–2.6)	.82 1.3 (.1–12.8)	.64 .8 (.3–2.2)
History of hypertension	159 (77.6)	.95 n/a	.07 .3 (.1–1.1)	.21 .3 (0–2.0)	.47 .7 (.2–2.0)
Current smoking	36 (17.6)	.44 1.9 (.4–10.4)	.39 1.8 (.5–7.3)	.70 1.6 (.2–15.6)	.19 2.1 (.7–6.4)
Atrial fibrillation	26 (12.7)	.97 n/a	.71 .7 (.1–5.5)	.47 2.3 (.2–23.4)	.39 .4 (.1–3.2)
Prior CEA	84 (41.0)	.07 2.0 (.9–4.4)	.04 2.0 (1.0–3.7)	.31 1.7 (.6–4.8)	.03 1.8 (1.1–3.1)
Restenosis after CEA	52 (25.4)	.85 1.2 (.2–6.3)	.29 2.0 (.5–7.5)	.98 1.0 (.1–9.6)	.26 1.9 (.6–5.4)
CHF	39 (19.0)	.52 1.7 (.3–9.3)	.48 1.6 (.4–6.5)	.76 1.4 (.1–14.1)	.26 1.9 (.6–5.7)
Prior MI	54 (26.3)	.47 .5 (.1–3.9)	.94 1.1 (.3–4.1)	.30 2.9 (.4–20.9)	.78 .8 (.3–2.7)
Prior CABG	82 (40.0)	.20 .2 (0–2.1)	.71 1.3 (.4–4.1)	.69 1.5 (.2–10.0)	.69 .8 (.3–2.2)
Prior TIA	69 (33.7)	.67 1.3 (.4–3.9)	.88 1.1 (.4–3.0)	.76 .7 (.1–5.7)	.91 1.0 (.5–2.4)
Prior stroke	50 (24.4)	.54 .5 (.1–4.3)	.01 5.0 (1.6–15.9)	.26 2.8 (.5–17.6)	.11 2.2 (.8–5.8)
PVD	44 (21.5)	.64 .6 (.1–5.1)	.06 3.3 (1.0–11.4)	.19 3.8 (.5–27.7)	.15 2.2 (.7–6.2)
CAD	120 (58.5)	.40 .5 (.1–2.4)	.33 2.0 (.5–7.6)	.51 2.2 (.2–21.1)	.59 1.3 (.5–3.7)
ESRD	8 (3.9)	.98 n/a	.38 2.7 (.3–23.9)	.98 n/a	.66 1.6 (.2–14.0)
COPD	33 (16.1)	.89 .9 (.1–7.4)	.31 2.1 (.5–8.2)	.63 1.8 (.2–17.5)	.39 1.7 (.5–5.5)
Contralateral occlusion	39 (19.0)	.75 .7 (.1–6.0)	.40 .4 (.1–3.3)	.76 1.4 (.1–14.1)	.43 .5 (.1–2.5)
Asymptomatic	139 (67.8)	.83 1.2 (.2–6.3)	.34 .6 (.2–1.9)	.45 .5 (.1–3.4)	.41 .7 (.2–1.8)
Close cell stent	49 (23.9%)	.05 4.5 (1.0–21.0)	.79 1.2 (.3–4.7)	.96 n/a	.26 1.8 (.6–5.3)

n/a = not applicable (patient did not have characteristic and outcome in question), TIA = transient ischemic attack, OR = odds ratio, CI = confidence interval, CHF = congestive heart failure, CABG = coronary artery bypass graft, PVD = peripheral vascular disease, CAD = coronary artery disease, ESRD = end stage renal disease, COPD = chronic obstructive pulmonary disease.

significance level. The fit of the model was assessed with the Hosmer and Lemeshow Goodness-of-Fit test,[32] where a *p*-value less than .05 indicated an ill-fit model.

Univariate analysis was also conducted for the DPF characteristics. Each DPF characteristic except concentricity was assumed a continuous variable taking the values given in Table 2. The rationale behind treating these variables as continuous is that it accounts for patient-to-patient variability for wall apposition, capture efficiency, and vascular resistance. It also accounts for variability in filter-to-filter manufacturing concerning porosity and pore density. Similar to the clinical variables, the association between each covariate and outcome was examined. The association between each variable (both clinical and DPF) was quantified for each TIA, stroke, neurologic-related death, and adverse event after 30 days.

Table 2 DPF[a] design characteristics.[26,31,32]

DPF	Accunet	Angioguard	FilterWire	Emboshield	Spider
Capture efficiency[b]	95.1	63.7	96.1	64.6	99.9
Vascular resistance[c]	24.8	30.6	12.8	14.7	3.5
Porosity[d]	4.5	11.3	12.9	2.2	50.4
Number of pores	912	1100	2576	400	1563
Pore density[e]	4.4	14.4	13.6	1.4	10
Wall apposition[f]	.075	4.2	.65	0	.49
Concentric	1	1	0	1	0

[a] DPF = distal protection filter.
[b] Capture efficiency = percentage of emboli captured by DPF.
[c] Vascular resistance measurements are expressed as a ratio of the vascular resistance in the ICA at full filter conditions normalized to the initial condition.
[d] Porosity is percentage of porous surface area to total surface area of DPF basket.
[e] Pore density is ratio of total number of pores to total surface area DPF basket.
[f] Wall apposition represented by a gap between the device and the arterial wall, expressed as a % of vessel cross-sectional area at the site of device deployment.

Results

The information from 208 procedures performed on 206 patients was collected for statistical analysis. Of the 208 patients included in the study, there were 2 MIs, 7 TIAs, 12 strokes, and 6 deaths in 20 patients. The 30-day all-cause stroke and death rate was 8.7% (12 strokes, 6 deaths: 18 events/208 patients). For asymptomatic patients, the 30-day all-cause stroke and death rate was 7.7% (7 strokes, 4 deaths: 11 events/142 patients), while for symptomatic patients it was 10.6% (5 strokes, 2 deaths: 7 events/66 patients). Five patients had a stroke and died within 30 days. The sixth patient died from a non-neurologic cause and was excluded from the analysis. Due to the low number of MI, it was also excluded from the analysis. In the final data set (i.e., excluding non-neurologic deaths and MI), the average age was 72-years ± 9 and almost two-thirds of the patients were male (66.8%) and asymptomatic (67.8%). The baseline characteristics are shown in Table 1. The 30-day stroke and neurologic death rate was 7.3% (11 strokes, 4 deaths: 15 events/205 patients). For asymptomatic patients, the 30-day stroke and neurologic death rate was 5.8% (6 strokes, 2 deaths: 8 events/139 patients), and for symptomatic patients it was 10.6% (5 strokes, 2 deaths: 7 events/66 patients). These stroke and death rates were higher than the American Heart Association (AHA) guidelines for carotid interventions (3% for asymptomatic patients; 6% for symptomatic patients).[33]

There were five different DPFs used in the 208 patients: Accunet, Angioguard, FilterWire, Emboshield, and Spider. Table 3 gives the distribution of the DPFs used during CAS. Due to the low number of patients treated with Emboshield ($n = 2$) and Spider ($n = 1$), they were excluded from the filter analysis. In addition, Emboshield now has an updated design, Emboshield NAV[6], further justifying its removal from the statistical treatment of the data. The earliest cases used Angioguard as this was the only DPF available at the time. With few exceptions, nearly all patients were treated with the manufacturer's recommended DPF-stent pair.

Univariate analysis yielded several variables that reached significance (see Table 1). Noteworthy are diabetes mellitus ($P = .04$, OR: 2.8, CI: 1.0—7.6) and prior CEA ($P = .03$, OR: 1.8, CI: 1.1—3.1) were significantly associated with adverse event. Peri-procedural stroke was significantly associated with prior CEA ($P = .04$, OR: 2.0, CI: 1.0—3.7) and prior stroke ($P = .01$, OR: 5.0, CI: 1.6—15.9), while peri-procedural TIA was significantly associated with closed-cell stents ($P = .05$, OR: 4.5, CI: 1.0—21.0).

Multivariate models were created with variables having a Wald statistic greater than 2 and non-significant Goodness-of-Fit p-value. Two models were created: adverse event within 30 days of CAS was associated with diabetes melliutus and prior CEA, while stroke within 30 days of CAS was associated with both prior stroke and CEA.

Subgroup analysis did not yield many statistically significant results, as shown in Tables 4 and 5. Asymptomatic patients with prior CEA were significantly associated with adverse events ($P = .04$, OR: 2.0, CI: 1.0—3.8) and symptomatic patients who had prior stroke were significantly associated with peri-procedural stroke ($P = .04$, OR: 11.3,

Table 3 DPF distribution.

DPF	Number (Percentage)	TIA	Stroke	Death	Adverse event
RX Accunet	86 (41.3)	2	4	1	7
Angioguard	69 (33.2)	1	5	4	6
FilterWire	50 (24.0)	4	3	0	6
Emboshield	2 (1.0)	0	0	1	1
Spider RX	1 (.5)	0	0	0	0

DPF = distal protection filter, TIA = transient ischemic attack.

Table 4 Asymptomatic patient characteristics and their *p*-value, odds ratio, and 95% confidence interval.

Characteristic	TIA *p-value* *OR* (95% CI)		Stroke *p-value* *OR* (95% CI)		Death *p-value* *OR* (95% CI)		Adverse Event *p-value* *OR (95% CI)*	
	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic
Age > 80 years	.97	.97	.91	.91	.22	.28	.64	.78
	n/a	n/a	1.1 (.1–10.2)	1.1 (.1–11.2)	5.9 (.4–97.4)	4.8 (.3–83.0)	.6 (.1–5.0)	.7 (.1–6.7)
Male	.16	.95	.29	.98	.96	.95	.17	.54
	.3 (0–1.7)	n/a	.4 (.1–2.1)	1.0 (.2–6.3)	n/a	n/a	.4 (.1–1.5)	1.7 (.3–9.6)
Diabetes mellitus	.19	.52	.93	.13	.58	.52	.21	.10
	3.4 (.5–21.1)	2.6 (.2–43.1)	1.1 (.2–6.1)	4.2 (.6–27.6)	2.2 (.1–35.8)	2.6 (.2–43.1)	2.3 (.6–8.4)	3.9 (.8–19.5)
History of dyslipidemia	.73	.72	.70	.92	.96	.72	.80	.77
	1.5 (.2–13.6)	.6 (0–10.0)	.7 (.1–4.1)	.9 (.1–5.8)	n/a	.6 (0–10.0)	.8 (.2–3.4)	.8 (.2–3.9)
History of hypertension	.96	.96	.08	.51	.33	.48	.43	.94
	n/a	n/a	.2 (0–1.2)	.5 (.1–3.5)	.2 (0–4.1)	.4 (0–6.1)	.6 (.1–2.3)	.9 (.2–5.3)
Current smoking	.16	.96	.95	.30	.97	.35	.22	.62
	3.8 (.6–24.2)	n/a	1.1 (.1–9.6)	2.7 (.4–18.2)	n/a	3.9 (.2–67.0)	2.5 .6–10.4)	1.6 (.3–9.1)
Atrial fibrillation	.97	.97	.97	.67	.97	.18	.96	.96
	n/a	n/a	n/a	1.7 (.2–16.8)	n/a	7.0 (.4–123.4)	n/a	1.1 (.1–10.0)
Prior CEA	.06	.95	.06	.27	.55	.29	.04	.32
	2.3 (1.0–5.6)	1.1 (.1–8.1)	2.2 (1.0–5.0)	1.9 (.6–6.2)	1.5 (.4–6.3)	2.6 (.4–14.7)	2.0 (1.0–3.8)	1.7 (.6–4.7)
Restenosis after CEA	.58	.97	.26	.73	.52	.97	.14	.91
	1.7 (.3–10.5)	n/a	2.6 (.5–13.4)	1.5 (.1–16.0)	2.5 (.2–41.2)	n/a	2.7 .7–9.8)	.9 (.1–8.2)
CHF	.87	.38	.97	.35	.26	.96	.81	.19
	1.2 (.1–11.3)	3.6 (.2–60.8)	1.0 (.1–8.6)	2.5 (.4–16.3)	5.0 (.3–82.2)	n/a	1.2 (.2–6.1)	2.9 (.6–14.9)
Prior MI	.66	.96	.26	.96	.95	.96	.42	.96
	.6 (.1–5.6)	n/a	2.6 (.5–13.4)	n/a	n/a	n/a	1.7 (.5–6.5)	n/a
Prior CABG	.35	.95	.70	.33	.80	.74	.47	.79
	.3 (0–3.2)	n/a	.7 (.1–4.0)	2.2 (.4–11.4)	1.4 (.1–23.6)	1.5 (.1–19.7)	.6 (.1–2.4)	1.2 (.3–5.4)
Prior TIA	.29	.84	.38	.23	.98	.32	.72	.39
	3.5 (.4–34.4)	1.2 (.2–8.3)	2.8 (.3–26.2)	.3 (.1–2.0)	n/a	.2 (0–3.9)	1.5 (.2–13.0)	.5 (.1–2.3)
Prior stroke	.93	.96	.12	.04	.37	.55	.53	.19
	.9 (.1–7.8)	n/a	3.2 (.7–14.1)	11.3 (1.2–108.3)	3.0 (.3–34.9)	2.4 (.1–39.9)	1.5 (.4–5.8)	3.6 (.7–17.8)
PVD	.93	.96	.11	.30	.36	.35	.15	.62
	.9 (.1–8.4)	n/a	3.9 (.8–20.5)	2.7 (.4–18.2)	3.7 (.2–61.4)	3.9 (.2–67.0)	2.6 (.7–10.1)	1.6 (.3–9.1)
CAD	.96	.94	.78	.24	.95	.93	.55	.82
	1.0 (.2–5.9)	n/a	1.3 (.2–7.3)	3.9 (.4–36.7)	n/a	.9 (.1–14.7)	1.5 (.4–6.2)	.2 (.2–5.9)
ESRD	.98	.99	.98	.07	.98	.99	.98	.12
	n/a	n/a	n/a	15.0 (.8–286.8)	n/a	n/a	n/a	9.7 (.5–175.1)
COPD	.80	.97	.95	.17	.97	.25	.71	.38
	1.3 (.1–12.6)	n/a	1.1 (.1–9.6)	3.9 (.6–26.4)	n/a	5.4 (.3–93.6)	1.4 (.3–6.9)	2.2 (.4–13.3)
Contralateral occlusion	.97	.35	.93	.96	.28	.96	.50	.64
	n/a	3.9 (.2–67.0)	.9 (.1–8.1)	n/a	4.7 (.3–77.9)	n/a	.5 (.1–4.0)	.6 (.1–5.3)

Close cell stent	.12 4.2 (.7–26.5)	.25 5.4 (.3–93.6)	.74 1.3 (.2–7.7)	.84 1.3 (.1–12.6)	.96 n/a	.97 n/a	.36 1.9 (.5–7.0)	.38 2.2 (.4–13.3)

n/a = not applicable (patient did not have characteristic and outcome in question), TIA = transient ischemic attack, OR = odds ratio, CI = confidence interval, CHF = congestive heart failure, CABG = coronary artery bypass graft, PVD = peripheral vascular disease, CAD = coronary artery disease, ESRD = end stage renal disease, COPD = chronic obstructive pulmonary disease.

CI: 1.2—108.3). Unexpectedly, patients with prior stroke were significantly associated with peri-procedural stroke, even though they were less than 80-years old ($P = .01$, OR: 7.3, CI: 1.7—30.5). Results for octogenarians were the same since one patient experienced stroke and death; there were no TIAs amongst octogenarians.

The DPF design characteristics analysis revealed some remarkable results (see Table 6). Neurologic death within 30 days of CAS was significantly associated with capture efficiency ($P = .004$), vascular resistance ($P = .04$), and wall apposition ($P = .004$). TIA within 30 days of CAS was significantly associated with vascular resistance ($P = .04$) and number of pores ($P = .046$). A second analysis that quantified the association between the DPF itself and outcome did not yield significant results.

Discussion

The statistically significant clinical variables obtained in the present investigation corroborate findings of previous studies. Recently, the results of the CREST (Carotid Revascularization Endarterectomy vs. Stenting Trial) were published, which randomized conventional risk patients 1:1 to surgical or endovascular treatment.[34] In this study, 96.1% of patients had embolic protection. Although there was no difference between CEA and CAS in the primary end point of MI, stroke, or death from any cause during the peri-procedural period or any ipsilateral stroke within 4 years after randomization ($P = .51$),[34] the CREST authors indicated that CAS is more effective in younger patients.[29,34] Although our study did not find a significant relationship between age and any of the outcomes investigated, younger patients with prior stroke were more likely to have a stroke within 30 days of CAS. Diabetes was also found significantly associated with adverse outcomes.[4,8] Previously, Malik et al. found an association between restenosis after CEA and minimal emboli generation, suggesting that cerebral protection may not be necessary for this subset of patients.[15] Touzé et al. found that patients who had carotid restenosis after CEA and treated with the use of a CPD had lower risk of stroke and death.[10] However, our investigation found a significant association between prior CEA patients and peri-procedural stroke and adverse events. Subgroup analysis indicated that patients who had prior stroke are at higher risk of having a stroke within 30 days of CAS, especially symptomatic patients and, surprisingly, patients less than 80-years old.

Although not statistically significant, peripheral vascular disease had an elevated OR for peri-procedural stroke (OR: 3.3, CI: 1.0—11.4). Elevated OR were found for asymptomatic patients with prior CEA who underwent peri-procedural TIA ($P = .06$, OR: 2.3, CI: 1.0—5.6) or peri-procedural stroke ($P = .06$, OR: 2.2, CI: 1.0—5.0). Closed cell stents also had an elevated OR for peri-procedural TIA in younger patients ($P = .06$, OR: 4.5, CI: 1.0—20.8).

This work advances previous statistical studies by the inclusion of DPF-specific design characteristics. Similar to previous studies that have quantified stent design parameters,[17—21] DPF design characteristics were quantified and postulated to have an effect on CAS outcome. To this end, numerous studies have used logistic regression to predict

Table 5 Octogenarian patient characteristics and their *p*-value, odds ratio, and 95% confidence interval.

Characteristic	TIA *p-value* *OR* (95% CI)		Stroke *p-value* *OR* (95% CI)		Death *p-value* *OR* (95% CI)		Adverse Event *p-value* *OR* (95% CI)	
	Octogenarian	Age < 80	Octogenarian	Age < 80	Octogenarian	Age < 80	Octogenarian	Age < 80
Male	n/a	.58	.95	.16	.95	.95	.95	.25
	n/a	.6 (.1–3.0)	n/a	.4 (.1–1.5)	n/a	n/a	n/a	.5 (.2–1.6)
Diabetes mellitus	n/a	.15	.47	.39	.47	.58	.47	.06
	n/a	3.0 (.7–14.2)	2.9 (.2–51.5)	1.8 (.5–7.0)	2.9 (.2–51.5)	2.2 (.1–36.0)	2.9 (.2–51.5)	2.8 (.9–8.0)
History of dyslipidemia	n/a	.996	.95	.29	.95	.51	.95	.31
	n/a	1.0 (.2–5.3)	n/a	.5 (.1–1.9)	n/a	.4 (0–6.4)	n/a	.6 (.2–1.7)
History of hypertension	n/a	.95	.34	.12	.34	.38	.34	.70
	n/a	n/a	.2 (0–4.4)	.3 (.1–1.3)	.2 (0–4.4)	.3 (0–4.7)	.2 (0–4.4)	.8 (.2–2.6)
Current smoking	n/a	.58	.99	.33	.99	.33	.99	.20
	n/a	1.6 (.3–8.6)	n/a	2.0 (.5–8.6)	n/a	4.0 (.2–65.6)	n/a	2.1 (.7–6.7)
Atrial fibrillation	n/a	.97	.34	.96	.34	.97	.34	.97
	n/a	n/a	4.2 (.2–76.6)	n/a	4.2 (.2–76.6)	n/a	4.2 (.2–76.6)	n/a
Prior CEA	n/a	.10	.92	.32	.92	.93	.92	.23
	n/a	1.9 (.9–4.1)	n/a	1.4 (.7–3.0)	n/a	n/a	n/a	1.4 (.8–2.5)
Restenosis after CEA	n/a	.92	.27	.49	.27	.96	.27	.44
	n/a	1.1 (.2–5.8)	5.2 (.3–97.6)	1.7 (.4–7.3)	5.2 (.3–97.6)	n/a	5.2 (.3–97.6)	1.6 (.5–5.0)
CHF	n/a	.32	.75	.54	.75	.97	.75	.20
	n/a	2.4 (.4–12.8)	1.6 (.1–27.8)	1.7 (.3–8.4)	1.6 (.1–27.8)	n/a	1.6 (.1–27.8)	2.2 (.7–7.6)
Prior MI	n/a	.62	.96	.99	.96	.37	.96	.84
	n/a	.6 (.1–4.9)	1.1 (.1–18.6)	1.0 (.2–5.1)	1.1 (.1–18.6)	3.6 (.2–58.9)	1.1 (.1–18.6)	.9 (.2–3.3)
Prior CABG	n/a	.23	.91	.65	.91	.71	.91	.75
	n/a	.3 (0–2.3)	.9 (.1–11.7)	1.4 (.4–5.3)	.9 (.1–11.7)	1.7 (.1–27.6)	.9 (.1–11.7)	.8 (.3–2.5)
Prior TIA	n/a	.62	.84	.95	.84	.95	.84	.93
	n/a	1.3 (.4–3.9)	1.3 (.1–15.3)	1.0 (.3–3.2)	1.3 (.1–15.3)	n/a	1.3 (.1–15.3)	1.0 (.4–2.5)
Prior stroke	n/a	.55	.53	.01	.53	.41	.53	.14
	n/a	.5 (.1–4.4)	2.1 (.2–19.9)	7.3 (1.7–30.5)	2.1 (.2–19.9)	3.2 (.2–52.7)	2.1 (.2–19.9)	2.3 (.8–6.9)
PVD	n/a	.62	.27	.11	.27	.37	.27	.28
	n/a	.6 (.1–4.9)	5.2 (.3–97.6)	3.0 (.8–11.9)	5.2 (.3–97.6)	3.6 (.2–58.9)	5.2 (.3–97.6)	1.9 (.6–5.9)
CAD	n/a	.45	.95	.55	.95	.84	.95	.80
	n/a	.6 (.1–2.5)	n/a	1.5 (.4–6.4)	n/a	.8 (0–12.2)	n/a	1.1 (.4–3.4)
ESRD	n/a	.98	n/a	.36	n/a	.98	n/a	.70
	n/a	n/a	n/a	2.8 (.3–25.5)	n/a	n/a	n/a	1.5 (.2–13.3)
COPD	n/a	.82	.98	.21	.98	.27	.98	.33
	n/a	.8 (.1–6.7)	n/a	2.5 (.6–10.7)	n/a	4.9 (.3–80.0)	n/a	1.8 (.5–6.2)
Contralateral occlusion	n/a	.92	.68	.96	.68	.97	.68	.33
	n/a	.9 (.1–7.7)	1.8 (.1–32.0)	n/a	1.8 (.1–32.0)	n/a	1.8 (.1–32.0)	.4 (0–2.9)
Asymptomatic	n/a	.87	.68	.39	.68	.58	.68	.45
	n/a	1.2 (.2–6.1)	.6 (0–9.7)	.6 (.1–2.1)	.6 (0–9.7)	.5 (0–7.4)	.6 (0–9.7)	.7 (.2–2.0)

Close cell stent	n/a	.06	.96	.53	.96	.96	.96	.15	
	n/a	4.5 (1.0–20.8)	n/a	1.6 (.4–6.7)	n/a	n/a	n/a	2.2 (.7–6.7)	

n/a = not applicable (patient did not have characteristic and outcome in question), TIA = transient ischemic attack, OR = odds ratio, CI = confidence interval, CHF = congestive heart failure, CABG = coronary artery bypass graft, PVD = peripheral vascular disease, CAD = coronary artery disease, ESRD = end stage renal disease, COPD = chronic obstructive pulmonary disease.

patient outcome following CAS. Iyer et al. reviewed retrospectively 3160 protected CAS cases treated with nine different CPDs.[23] Eccentric filters (FilterWire, Spider) were used in 60.4% of procedures, concentric filters (Emboshield, Angioguard, Trap, Accunet) were used in 32.4%, and the rest used balloon devices. There was no statistically significant difference in the risk for having a procedural adverse event as compared to FilterWire, the most frequently used device. However, there was an increased 30-day adverse event rate for Accunet as compared to FilterWire ($P = .05$). Pairwise comparisons of device type revealed that there was no significant difference in the risk of having an adverse event 30-days post-procedure. There was an increased risk for eccentric filters over concentric filters ($P = .04$), however, when adjusting for risk factors and stent type, there was no difference.

One recent study attempted to differentiate patient outcome based on DPF used.[22] The analysis used clinical data and was based upon peri-procedural flow impairment of three DPFs (Angioguard, FilterWire, Spider). Flow obstruction occurred more frequently with the use of Angioguard over FilterWire and Spider. All the procedures experiencing no flow occurred with Angioguard. Elevated odds ratio was found for open-cell stent designs and concentric DPFs.[2] The authors concluded that further analysis of device design variables needs to be investigated; in particular for symptomatic patients or those with echolucent lesions, the use of closed-cell stents and eccentric CPDs may be warranted. It is important to note that analysis of binary attributes such as open- or closed-cell stents or one-dimensional measures such as cell size can be misleading due to unaccounted for design characteristics.[19]

The assessment of DPF design characteristics and patient outcome in this work revealed that capture efficiency had a significant association with patient outcome after 30 days. Having a high capture efficiency being beneficial for patient outcome is intuitive; it is likely that less debris travels to the intracranial circulation and causes a neurologic event. A high vascular resistance indicates decreased blood flow to the brain, which can result in a neurologic occurrence. The number of pores is another indicator of the amount of blood flow; the more pores, the more blood reaches the brain through the ICA. Poor wall apposition can have a negative effect on patients due to plaque emboli potentially occurring between the DPF and the artery wall downstream. Concentricity was not found to be significantly associated with any of the outcomes. This finding disagrees with the work of Hart et al. in which eccentric filters were considered superior to concentric filters[2] but agrees with Iyer et al. in which there was no statistical difference between eccentric and concentric filters.[23] In addition, vascular resistance and number of pores had an indeterminate effect on patient outcome. Porosity and pore density were not significant, although these measures have an effect on vascular resistance, which was positively associated with procedural death. Thus, our hypothesis proved to be partially true; high capture efficiency DPFs are beneficial for patient outcome, while parameters quantifying the effect of a DPF on local blood flow conditions have an indeterminate or negative effect.

Due to one DPF used more than others during consecutive periods, operator experience could play a role, with

Table 6 DPF design characteristics and statistical significance ($P < .05$).

Design Characteristic	TIA	Stroke	Death	Adverse Event
Capture Efficiency	.24	.42	.004	.93
Vascular Resistance	.04	.86	.04	.44
Porosity	.31	.36	.19	.25
Number of Pores	.046	.74	.40	.26
Pore Density	.56	.32	.06	.31
Wall Apposition	.37	.37	.004	.79
Concentric	.06	.83	.96	.29
OR (95% CI)	.2 (.1—1.1)	.9 (.2—3.4)	n/a	.6 (.2—1.6)

DPF = distal protection filter, OR = odds ratio, CI = confidence interval.

more favorable results occurring the more the device was used. However, since an experienced interventionist with 20+ years of experience treated all patients, the operator effect should be minimal. Furthermore, as Iyer noted,[23] adjusting for stent type for each DPF can change the relative risk of procedural adverse events. Since nearly all cases used the manufacturer's recommended stent-DPF pair, such analysis would not be useful.

There are several limitations associated with the current investigation. It is important to note that the calculated associations quantify a measure of probability that the outcome will occur; it does not give a direct cause-and-effect relationship. Associations between variables can be found although they may not make clinical sense. Thus, predictions made by these statistic analyses need to be interpreted with care. This study was a retrospective analysis based on existing medical records, which were recorded for reasons other than research. For this reason, it is possible that a retrospective study will miss important contributing factors. However, hypotheses can be generated for future, prospective studies to investigate further cause-and-effect relationships. In addition, patients included in this study were treated at a single center (UPMC). A multiple center study would be more representative of the overall CAS patient population due to exclusion of systematic reporting biases or policies on patient treatment. Finally, this study should benefit from the inclusion of more patient data; if the patient population is large enough, a multivariate logistic regression equation can be derived. The size of the patient population is dependent upon the number of covariates examined simultaneously.[32] Assuming a 3% or 6% adverse event rate (AHA's target stroke and death rate for asymptomatic and symptomatic patients undergoing repair, respectively)[33] and three simultaneous covariates, the patient population should be between 500 and 1000 subjects. A multivariate logistic regression equation has the advantage of examining multiple variables simultaneously and quantifying interactions between variables (e.g., the relationship between hypertension, current smoking, and dyslipidemia).

Conclusion

A retrospective analysis of clinical variables can provide valuable information for rigorous patient selection that can yield a favorable CAS outcome. This study serves as a preliminary investigation to determine factors that are influential on patient outcome. Future studies with a larger sample size will yield more statistically significant results, particularly to assess the effect of DPF design characteristics. Design parameters that correlate with adverse outcomes can be avoided in designs of future device generations.

Author Contributions

GMS and EAF developed the conception and design of the study and wrote the manuscript. GMS and RTK were responsible for the statistical analysis and interpretation of results. Data was collected by GMS and MHW. The manuscript was critically revised by RTK and EAF, and final approval granted by MHW and EAF.

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