Cerebral embolic protection in thoracic endovascular aortic repair

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ABSTRACT

Background: Stroke occurs in 3% to 8% and silent cerebral infarction in >60% of patients undergoing thoracic endovascular aortic repair (TEVAR). We investigated the utility of a filter cerebral embolic protection device (CEPD) to reduce diffusion-weighted magnetic resonance imaging (DW-MRI) detected cerebral injury and gaseous and solid embolization during TEVAR.

Methods: Patients anatomically suitable underwent TEVAR with CEPD, together with intraoperative transcranial Doppler to detect gaseous and solid high-intensity transient signals (HITSs), pre- and postoperative DW-MRI, and clinical neurologic assessment ≤6 months after the procedure.

Results: Ten patients (mean age, 68 years) underwent TEVAR with a CEPD. No strokes or device-related complications developed. The CEPD added a median of 7 minutes (interquartile range [IQR], 5-16 minutes) to the procedure, increased the fluoroscopy time by 3.3 minutes (IQR, 2.4-3.9 minutes), and increased the total procedural radiation by 2.2%. The dose area product for CEPD was 1824 mGy·cm^2 (IQR, 1235-3392 mGy·cm^2). The average contrast volume used increased by 23 mL (IQR, 24-35 mL). New DW-MRI lesions, mostly in the hindbrain, were identified in seven of nine patients (78%). The median number was 1 (IQR, 1-3), with a median surface area of 6 mm^2 (IQR, 3-16 mm^2). A total of 2835 HITSs were detected in seven patients: 91% gaseous and 9% solid. The maximum number of HITSs were detected during CEPD manipulation: 142 (IQR, 59-146; 95% gaseous and 5% solid). The maximum number of HITSs during TEVAR occurred during stent deployment: 82 (IQR, 73-142; 81% gas and 11% solid). Solid HITSs were associated with an increase in surface area of new DW-MRI lesions ($r_s = 0.928$; $P = .01$). Increased gaseous HITSs were associated with new DW-MRI lesions ($r_s = 0.912$; $P = .01$), which were smaller (<3 mm; $r = 0.88$; $P = .02$). Embolic debris was captured in 95% of the filters. The median particle count was 937 (IQR, 146-1687), and the median surface area was 2.66 mm^2 (IQR, 0.08-9.18 mm^2).

Conclusions: The use of a CEPD with TEVAR appeared to be safe and feasible in this first pilot study and could serve as a useful adjunct to reduce cerebral injury. The significance of gaseous embolization and its role in cerebral injury in TEVAR warrants further investigation. (J Vasc Surg 2018;68:1656-66.)

Keywords: CEPD; DW-MRI; Embolization; HITS; TEVAR

A sharp increase has occurred in interventional treatment for thoracic aortic disease.[1] Thoracic endovascular aortic repair (TEVAR) has been adopted as the standard treatment method for thoracic aortic disease over open surgical repair, because the need for thoracotomy and aortic cross-clamping are avoided, morbidity is reduced, and the hospital stay is significantly decreased.[2] However, stroke remains a significant periprocedural complication, with reported rates of 3% to 8%,[3,4] and associated early mortality.[4]

Cerebral microembolization during aortic arch instrumentation has been shown to be the primary cause of perioperative stroke during TEVAR.[3] Transcranial Doppler (TCD) studies, using real-time detection of microembolic high-intensity transient signals (HITSs) in the middle cerebral arteries, have detected embolization during both the diagnostic and the treatment phases of TEVAR, with a clear association between the total number of HITSs and the occurrence of subsequent stroke, transient ischemic attack, and death.[5] Recent neuroimaging studies[6,7] showed that >60% of patients undergoing TEVAR have new "silent" ischemic lesions detected by magnetic resonance imaging (MRI), with an associated persistent early neurologic deficit on neuropsychometric testing of older patients.[7]

Silent cerebral infarction (SCI) is image-proven brain injury of ischemic etiology in patients with no focal neurologic abnormality. These lesions have been identified as

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independent predictors of future stroke (increasing the risk by two- to fourfold), dementia, depression, and cognitive impairment.[8-10] The volume of subclinical embolic infarct on MRI has been linked to worse short- and long-term verbal reasoning and memory scores after carotid revascularization.[11]

Cerebral embolic protection devices (CEPDs) have been used as adjuncts in other endovascular procedures such as transcatheter aortic valve insertion (TAVI) to reduce the risk of brain injury.[12,13] The Sentinel cerebral protection system (CPS; Claret Medical Inc, Santa Rosa, Calif) is a dual filter CEPD designed to protect the brachiocephalic trunk and left common carotid artery. Randomized controlled trials with a CEPD in TAVI have shown a significant decrease in the number and volume of new SCI lesions,[12,13] with an associated early improved neurologic outcome.[14] Embolic debris have been captured in the filters in 97% of TAVI cases.[15]

The use of cerebral embolic protection in TEVAR and its impact on cerebral embolization and ischemic brain injury have not been investigated previously. To the best of our knowledge, the present clinical pilot study is the first to evaluate the safety and feasibility of using a CEPD in TEVAR and its effect on gaseous and solid embolization, MRI-detected brain injury, and the clinical stroke rate.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, prospective cohort pilot study
- **Take Home Message:** In 10 patients, a filter cerebral embolic protection device (CEPD) was used during thoracic endovascular aortic repair procedures, there were no strokes, and 95% of the CEPDs captured embolic debris.
- **Recommendation:** The results of the present study suggest that the use of a CEPD during thoracic endovascular aortic repair could reduce the incidence of cerebral injury.

METHODS

Patient selection. The UK National Research Ethics Service Committee London-Fulham approved the present study (08/H0711/59), as did the institutional National Health Service Trust New Devices Committee. All patients gave written informed consent for CEPD insertion and tissue analysis of the debris captured in the filters.

Sentinel CPS. The Sentinel CPS is a 6-French, 100-cm long, steerable sheath comprising two conical filters made of a 140-μm pore biocompatible polyurethane film. It is navigated over a 0.014-in. wire. The device is inserted using a right radial or brachial access under fluoroscopic guidance. The proximal filter is first deployed at the origin of the brachiocephalic trunk. The distal segment of the catheter can then articulate to navigate through the aortic arch and into the left common carotid artery for deployment of the distal filter (Fig 1, *A*). At the end of the TEVAR, the steps are reversed, and the filters are captured back into the catheter and retrieved.

Eligibility for Sentinel protection device. Patients undergoing TEVAR as an elective or emergency procedure for any thoracic aortic pathology at a tertiary referral vascular unit in London, UK, were screened for eligibility for insertion of the Sentinel CEPD. The Vascular P-Possum score was calculated to predict for morbidity and mortality. The inclusion criteria were proximal landing zones 2, 3, and 4 according to Ishimaru's classification[16] (Fig 1, *B*). Landing zones 0 and 1 were excluded to ensure the device would not be trapped by the thoracic endograft on deployment. The device in situ is shown in Fig 1, *C*.

The aortic arch anatomy had to match the anatomic sizing requirements for the Sentinel CPS. The diameter of the origins of the brachiocephalic trunk and left common carotid artery should range from 9 to 15 mm and 6.5 to 10 mm, respectively, without excessive tortuosity or >70% obstructive atherosclerotic disease. All elective cases had undergone preoperative carotid duplex ultrasonography to assess for any significant stenosis. All emergency patients underwent anatomic assessment using preoperative computed tomography aortography (CTA). The exclusion criteria were any contraindication to MRI or a procedure time >180 minutes to reduce risk of thrombus formation on the filter.

Preoperative evaluation of aortic atheroma. All patients underwent preoperative CTA (Brilliance iCT 256-slice scanner; Philips Healthcare, Amsterdam, Netherlands) in accordance with standard clinical protocol, with a 1-mm slice thickness and intravenous iodinated contrast. An interventional radiologist, unaware of whether the patient was receiving cerebral embolic protection, graded the disease in the aortic arch and descending thoracic aorta. Atheroma was quantitatively graded according to the thickness: grade 1, normal; grade 2, intimal thickening; grade 3, atheroma ≤5 mm; grade 4, >5 mm; and grade 5, mobile lesion.[17]

MRI studies. Cerebral MRI was performed using the 3.0 Tesla Discovery MR750w system (GE Healthcare, Buckinghamshire, UK). The MRI protocol consisted of three sequences: axial diffusion-weighted imaging (DWI) array spatial sensitivity encoding technique (slice thickness, 5 mm; gap 1 mm); axial T2-weighted fluid-attenuated inversion recovery (slice thickness, 5 mm; gap 1 mm); and coronal T1-weighted fast spoiled gradient echo three-dimensional (slice thickness, 1 mm; no gap).

Preoperative diffusion-weighted (DW)-MRI was performed to exclude the presence of any preexisting lesions.

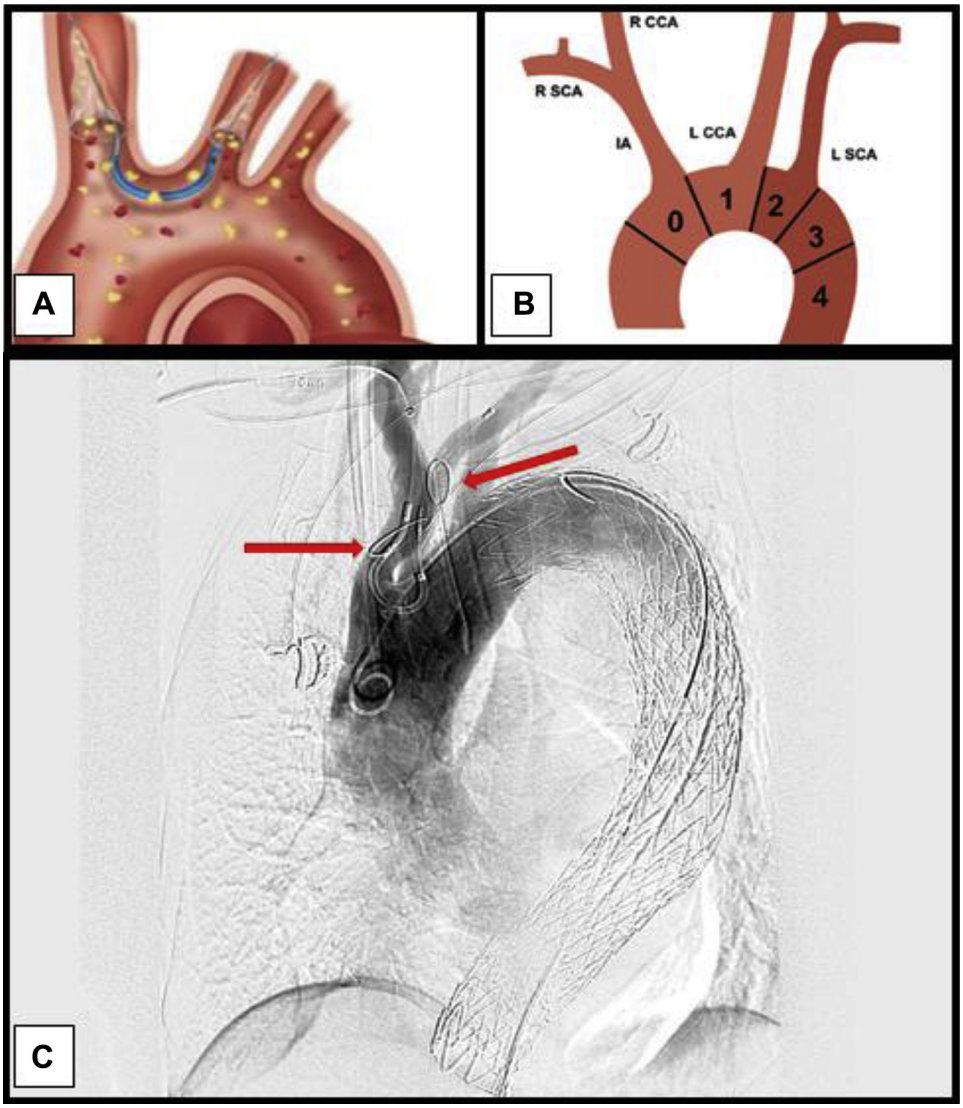

Fig 1. A, The Sentinel cerebral protection system. **B,** Proximal landing zones (PLZ) for thoracic endovascular aortic repair (TEVAR) in the aortic arch. PLZ 0-1, unsuitable for device use; PLZ 2-4, suitable for device use. **C,** The Sentinel cerebral protection system in situ with TEVAR. *Arrows* point to the proximal and distal filters of the cerebral embolic protection device (CEPD). *IA,* Innominate artery; *L CCA,* left common carotid artery; *L SCA,* left subclavian artery; *R CCA,* right common carotid artery; *R SCA,* right subclavian artery.

Chronic small vessel ischemia was classified using the Fazekas scale.[18] Postoperative MRI was performed within 72 hours or as soon as the clinical condition of the patient allowed.

The number, territory, maximum diameter, and maximum surface area of each new lesion were analyzed by two experienced neuroradiologists who were unaware of CEPD insertion and clinical outcomes. The lesion surface area (r_s) was measured on the slice with the largest lesion diameter. Lesions were considered separate if no continuity was found between them on the same slice or on adjacent slices. The brain was divided into predefined vascular territories: anterior circulation (AC) of the anterior cerebral artery and middle cerebral artery (MCA) and the posterior circulation (PC), including the vertebrobasilar and posterior cerebral artery territories. The border zone "watershed" territories of dual blood supply were also defined.[19]

Intraprocedural TCD assessment. Cerebral embolization detection was performed using bilateral TCD insonation of the MCA with multifrequency automated embolus detection software (EmboDop DWL; Compumedics Ltd, Dresden, Germany). The TCD insonates simultaneously with 2.0- and 2.5-MHz frequencies to differentiate between gaseous and solid emboli through an automated calculation of ratios of reflected ultrasound power. This has been assessed and validated using in vivo and in vitro studies.[20]

The TCD signal was continuously recorded during all phases of each procedure, including manipulation of the CEPD. Independent manual offline analysis was performed by two trained observers for identification of HITSs, and each signal was characterized as gaseous or solid emboli. Solid emboli tend to appear lower in the spectral waveform, to have reduced ultrasound reflectivity, and to have a shorter duration of travel with reduced acoustic impedance compared with gaseous emboli[21] (Fig 2, *A*). Using these criteria, both observers counted gaseous and solid emboli using a combination of the machine count and manually characterizing each individual embolus to ensure rejection of artifacts and increase the sensitivity and specificity. In the case of "clusters" of embolic showers during deployment of the stents or angiography contrast runs (Fig 2, *B*), it was not possible to perform an individual count, and the machine count was used. Interobserver reliability was calculated for total HITSs and for differentiation of emboli.

Neurologic assessment. The same trained assessor performed a neurologic examination preoperatively and at 6 weeks and 6 months postoperatively. The functional neurologic outcome was scored using the modified Rankin scale.

TEVAR procedure. All cases were performed with the patient under general anesthesia, and intravenous heparin was administered to maintain an activated clotting time of 250 seconds. All patients received the Gore c-TAG thoracic stent-graft (W. L. Gore & Associates, Flagstaff, Ariz) with a CEPD using right brachial artery access. All stents were manipulated over a standard 0.035-inch, curved-tip J-wire and stiff Amplatz wire. The thoracic stents were flushed with saline before deployment as per standard procedure.

Histopathologic examination. All filters retrieved from the delivery system were stored in a 10% neutral-buffered formalin solution and sent to a histopathology core laboratory (CV Path, Santa Rosa, Calif) for analysis. Debris composition and morphometric analysis were performed, and the particle count, diameter, and surface area were recorded.

Statistical analysis. Statistical analysis was performed using SPSS software, version 22 (IBM Corp, Armonk, NY). Continuous variables are presented as the median (interquartile range [IQR]) and categorical variables as frequencies and percentages. The spread of data was nonparametric, and comparisons were made using Spearman's rank correlation coefficient, Friedman's test and the Wilcoxon signed-rank test, with $P < .05$ considered statistically significant. Logarithmic transformation of non-normally distributed variables was used as required. Bonferroni's correction was used to determine the statistical significance on multiple tests. Cronbach's α was used to assess the inter-rater reliability.

RESULTS

From September 2015 to May 2016, 22 patients underwent TEVAR. Of the 22 patients, 13 were anatomically suitable for CEPD and 10 underwent TEVAR (Gore c-TAG) with embolic protection. Three patients were not recruited for the present study because they were clinically unstable on admission or had a contraindication to MRI. One patient had a history of stroke. Of the 10 cases, seven were performed as urgent cases. The median Vascular-POSSUM score for the predicted risk of mortality was 8.2% (IQR, 4.6%-19.1%) and for morbidity was 70.9% (IQR, 56.2%-87.8%; Table).

Procedural and safety data. Complete device success, defined as successful deployment and retrieval of both the proximal and distal filters, was achieved in nine patients. In one patient treated on an emergency basis, the distal filter could not be deployed owing to suboptimal imaging visualization in the operating theater. All other procedures were performed in a dedicated vascular hybrid suite. No complications developed from use of the Sentinel CPS.

The CEPD added a median of 7 minutes (IQR, 4.6-16 minutes) to the procedure, increased the fluoroscopy time by 3.3 minutes (IQR, 2.4-3.9 minutes), and increased the total procedural radiation dose by 2.2%. The dose area product for the CEPD was 1824 mGy·cm^2 (IQR 1235-3392 mGy·cm^2). The average contrast volume used increased by 23 mL (IQR, 24-35 mL).

Clinical outcomes. No patient had significant (>50%) stenosis on carotid duplex ultrasonography or CTA. All stent-grafts were deployed satisfactorily. One patient required an emergency carotid-carotid bypass owing to intraprocedural proximal stent migration. The patient recovered well with no clinical neurologic deficit postoperatively.

The 30-day mortality and major adverse cardiac and cerebrovascular event rate was 0%, with no cases of stroke. One patient died on day 13 postoperatively of sepsis related to a spinal abscess. The patient included in the study with a previous stroke had no new neurologic deficits after the procedure. The median length of stay was 15 days (IQR, 7-21 days). The median follow-up duration was 6.6 months (IQR, 5.3-8 months).

Intraoperative TCD embolization. TCD monitoring was performed on seven patients with satisfactory temporal bone windows, with bilateral insonation of the MCA achieved in five patients and only the left MCA insonated in two patients owing to limited ultrasound windows.

The median number of total HITSs was 453 (IQR, 227-521), with a median number of solid emboli of 32 (IQR, 17-54) and median number of gaseous emboli of 391 (IQR, 213-461). The inter-rater reliability between the two assessors was excellent, with a Cronbach's α of 0.98 and 0.99.

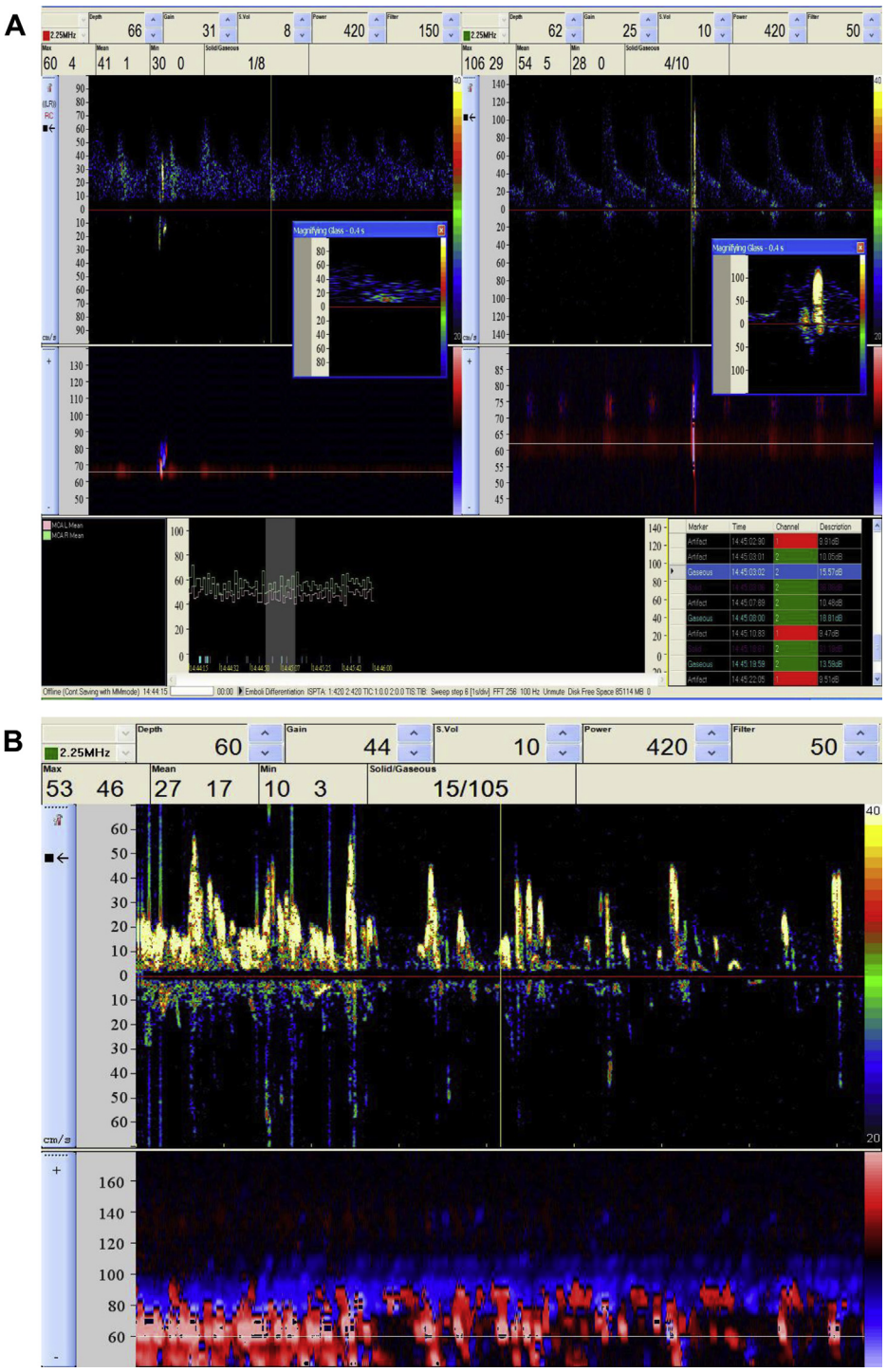

Fig 2. A, Trancranial Doppler (Embodop DWL): *left,* solid embolus; *right,* gas embolus. **B,** Embolic cluster of high-intensity transient signals (HITSs).

The maximum HITSs were observed during CEPD manipulation and deployment, with a median of 124 (IQR, 59-146), of which 95% were gaseous and 5% were solid. The maximum HITSs during TEVAR occurred during stent manipulation and deployment (median, 82; IQR, 73-142), of which 89% were gaseous and 11% were solid. The maximum relative proportion of solid to gaseous HITSs was noted in the wire and pigtail manipulation phase (13%) and at stent manipulation and deployment (11%; Fig 3, *A*). Four patients underwent adjunctive surgery in the form of carotid-carotid and left carotid-subclavian bypass, with only the left MCA insonated during surgery.

Table. Patient demographic and procedural data (N = 10)

Variable	No. (%)
Age, years	68 (46-85)
Male sex	7 (70)
Emergency	7 (70)
Etiology	
Aneurysmal descending thoracic aorta	5
Thoracic aortic aneurysm	1
Thoracoabdominal aortic aneurysm	1
Chronic type B dissection and dilated aorta	2
Mycotic aneurysm	1
Acute aortic syndrome	5
Acute type B dissection	2
Intramural hematoma	3
Patient comorbidities	
Previous stroke	1 (10)
Hypertension	10 (100)
Hypercholesterolemia	9 (90)
Diabetes mellitus	1 (10)
Smoking history	7 (70)
Ischemic heart disease	1 (10)
Respiratory disease	5 (50)
Cancer	2 (20)
Previous cardiovascular or aortic surgery	3 (30)
Atrial fibrillation	2 (20)
Drug history	
Antiplatelet	4 (40)
Statin	8 (80)
Chronic kidney disease	
Normal (eGFR >90 mL/min)	8 (80)
Mild (eGFR 60-89 mL/min)	1 (10)
Severe (eGFR >90 mL/min)	1 (10)
Procedure	
TEVAR	6
Arch hybrid	4
TEVAR with left carotid-subclavian bypass	3
TEVAR with carotid-carotid and left carotid-subclavian bypass	1
Proximal landing zone	
Zone 2	4 (40)
Zone 3	6 (60)
Grade atheroma of aortic arch	
1-2	7 (70)
3-4	3 (30)
Baseline disease burden on MRI (Fazekas scale)	
Mild	9
Moderate	1

eGFR, Estimated glomerular filtration rate; *MRI*, magnetic resonance imaging; *TEVAR*, thoracic endovascular aortic repair.

DW-MRI study. Of the 10 patients, nine underwent pre- and postoperative brain MRI but one required a postprocedural permanent pacemaker, and MRI was therefore contraindicated. The median interval to postoperative MRI was 2 days (IQR, 2-4.5 days). The independent-blinded analysis of the lesion number and surface area by two neuroradiologists was excellent, with a Cronbach's α of 0.97 and 0.98. Of these nine patients, two did not have evidence of any new DWI lesions. However, 23 new DWI lesions were noted in seven patients. The median number of lesions was 1 (IQR, 1-3), and the median surface area was 6 mm^2 (IQR, 3-16 mm^2). Of these 23 lesions, six (26%) were <3 mm in the maximum diameter and 17 (74%) were ≥3 mm. A more diseased aortic arch (grade 3 and 4) was associated with an increase in lesions with a diameter ≥3 mm ($r = 0.663$; $P = .05$) but had no significant effect on the total MRI lesion number or surface area (Fig 3, *B*).

An increase in total HITSs was associated with an increased number of MRI lesions ($r_s = 0.912$; $P = .01$) but had no effect on the total lesion surface area ($r_s = 0.580$; $P = .23$). A trend was seen toward an increase in number ($r_s = .794$; $P = .06$) and a significant increase in surface area ($r_s = .928$; $P = .01$) of new DW-MRI lesions noted with an increase in the number of solid emboli (Fig 3, *C*). The number of gaseous emboli was associated with more MRI lesions ($r_s = 0.912$; $P = .01$) and showed a positive correlation with the number of lesions <3 mm in diameter ($r = 0.88$; $P = .02$) but did not have an effect on lesion surface area ($r_s = 0.638$; $P = .17$; Fig 3, *D*).

The distribution of the lesions per vascular territory is shown in Fig 4, with 15 of 23 (65%) in the PC, six of 23 (26%) in the AC, and two of 23 (9%) in the temporo-occipital border-zone territory supplied by either the posterior cerebral artery or MCA.

Histopathologic findings. A total of 19 filters (10 proximal and nine distal) were analyzed. Debris was captured in 18 of the 19 filters (95%). All proximal (100%) and most distal (89%) filters contained debris. The most frequent debris composition was acute thrombus (95%), arterial wall (63%), and foreign material (32%; Fig 5, *A* and *B*).

The median total number of particles captured was 937 (IQR, 146-1687), and the median total surface area of all particles captured was 2.66 mm^2 (IQR, 0.08-9.18 mm^2). The proximal filters captured more particles than did the distal filters (1648 vs 480). However, the distal filters contained tissue with a greater total surface area (3,338,928 μm^2 vs 2,411,789 μm^2) and captured larger tissue fragments with a larger average particle surface area (6958 μm^2 vs 1461 μm^2; Fig 5, *C* and *D*). A trend was seen toward an increase in the total surface area of

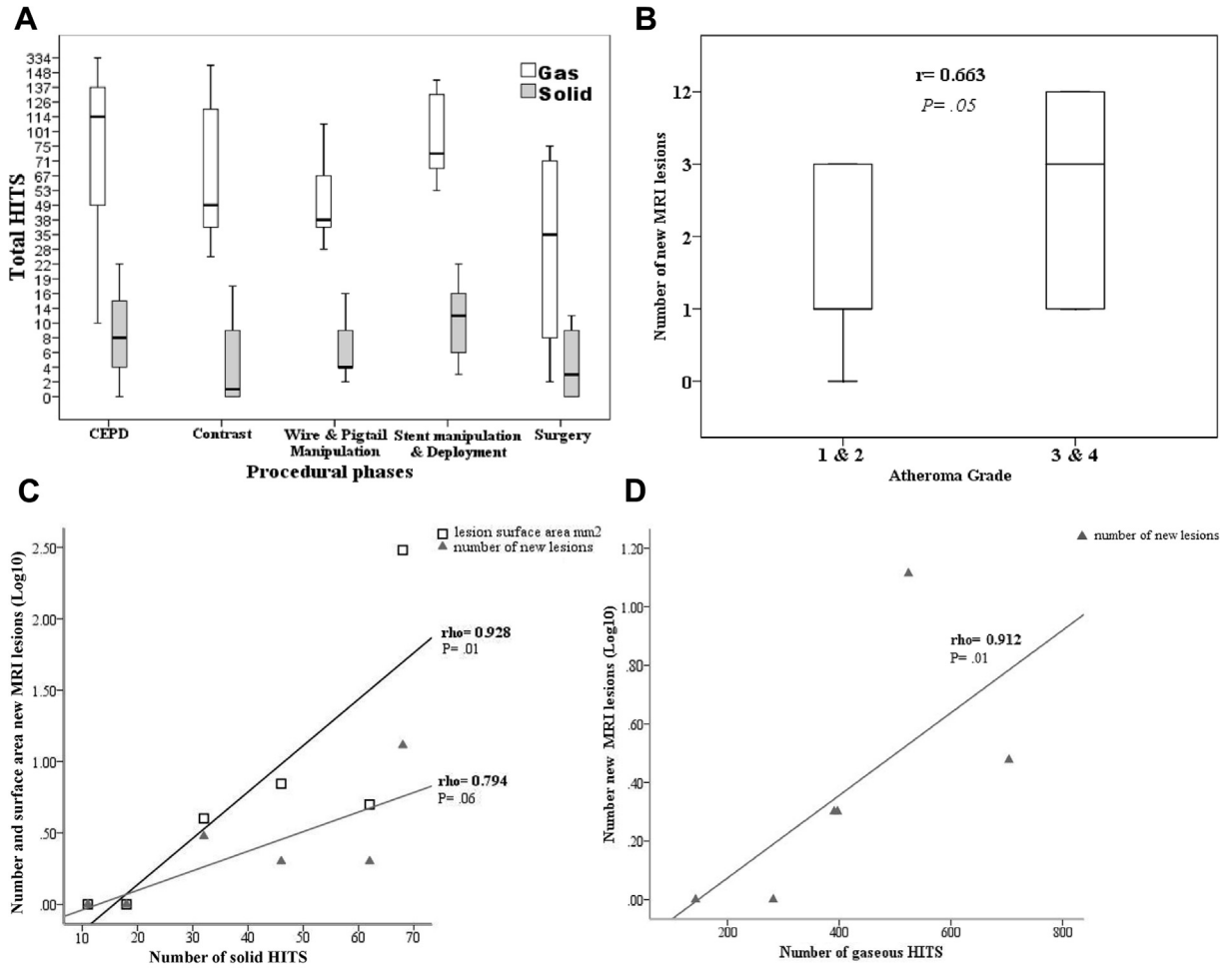

Fig 3. **A,** Procedural solid and gaseous high-intensity transient signals (HITSs). **B,** Pearson's correlation between new magnetic resonance imaging (MRI) lesions ≥3 mm in diameter and grade of atheroma on the aortic arch. **C,** Spearman's rank correlation between number of solid HITSs and number and surface area of new MRI lesions. **D,** Spearman's rank correlation between the number of gaseous HITSs and number of new MRI lesions.

the particles captured and larger diameter particles (>150 μm) in patients not previously receiving antiplatelet therapy ($r = 0.56$, $P = .08$; and $r = 0.459$, $P = .18$).

DISCUSSION

To the best of our knowledge, the present pilot study is the first to describe the use of cerebral embolic protection in TEVAR. In multiple clinical studies, the learning curve associated with the use of the Sentinel CPS has been between three and five cases.[12,13] Our results indicated a reduction in new cerebral infarcts compared with two previously reported neuroimaging studies of unprotected TEVAR.[6,7] The patients recruited had no evidence of clinical postprocedural neurologic deficit, device-related complications, or major adverse cardiac and cerebrovascular event. Device success was 90%, in keeping with the TAVI experience in larger trials (90% and 94.4%).[12,13] The use of the filter added ~7 minutes to the procedure, an additional 3 minutes of fluoroscopy time, and a 2% increase in the radiation dose. The CLEAN-TAVI (Claret Embolic Protection and TAVI)[12] and SENTINEL[13] studies reported procedural times of 18 and 13 minutes, respectively, with a similar addition of fluoroscopy time.

The apparent reduction in the number of DW-MRI-detected new brain lesions with the use of a CEPD in TEVAR is encouraging. We identified 23 new lesions in seven of nine patients (78%), with median surface area of 6 mm^2. Most were in the hindbrain supplied by the PC (65%) compared with the AC (26%). Kalhert et al[6] identified 29 new DWI lesions in 12 of 19 patients (63%) undergoing TEVAR without protection, mostly in the AC (66%), with a median lesion volume of 90 mm^3. The use of 3.0 Tesla MRI in the present study would be expected to improve the sensitivity for lesion detection compared with the 1.5 Tesla MRI used by Kalhert et al.[6] Even after allowing for such differences between studies, the use of embolic protection appears to reduce the size and distribution of lesions, suggesting improved protection for the AC (Fig 4).

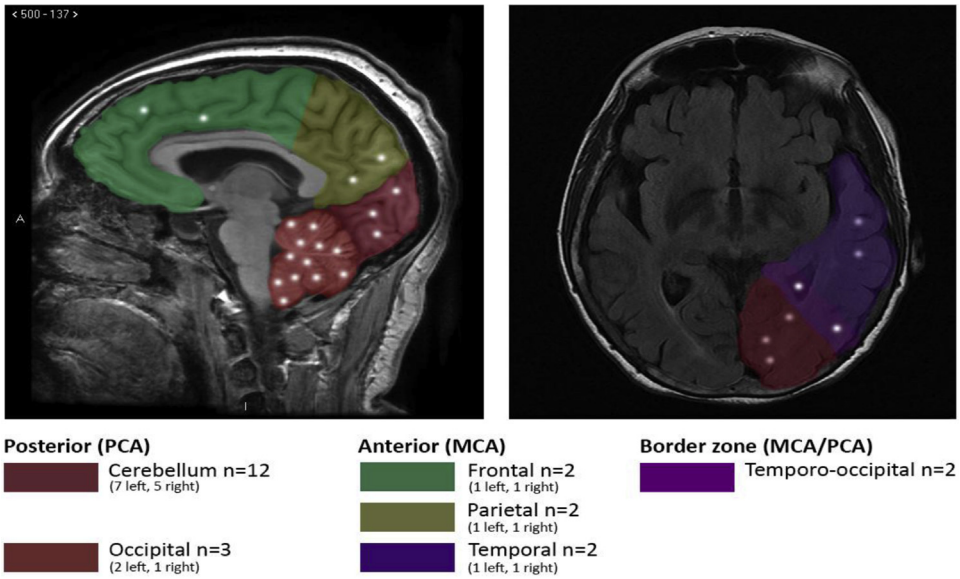

Fig 4. Territories of new magnetic resonance imaging lesions. *MCA,* Middle cerebral artery; *PCA,* posterior cerebral artery.

The rate of embolic debris capture "en route" to the brain was high (95%), similar to the experience with TAVI (97%),[15] with an average of 0.54 mm^2 of embolic material captured per patient. The filters from the emergently treated patients who had been receiving previous antiplatelet therapy showed a trend toward an increased surface area and diameter of particles captured. Embolic protection might provide benefit in emergency situations in which optimal antithrombotic conditions have not been achieved.

To the best of our knowledge, the present study is the first to differentiate microemboli in TEVAR into gaseous or solid lesions to identify the greatest risk phases of the procedure, with MRI correlation. The putative mechanism of brain injury in TEVAR is disruption of atherosclerotic plaque into the cerebral circulation through manipulation of large delivery systems in a diseased aortic arch and the sudden apposition of the stent graft to the aortic wall during deployment.[3,4] However, data have been conflicting regarding the role of solid and gaseous emboli in the development of ischemic MRI lesions and neurologic decline in the interventional setting, with reports implicating both solid[22] and gaseous[23,24] embolization.

The greatest rate of embolization was seen during manipulation of the CEPD itself, with a median number of HITSs of 142 (IQR, 59-146). Of these, most were gaseous (95%). Similar to the findings reported by Bismuth et al,[5] we have demonstrated intracranial embolization detected at the MCA during all phases of TEVAR, with maximum HITSs and embolic "showers" (Fig 2, *B*) observed during stent deployment (26%), with most characterized as gaseous (81%). The maximum proportion of solid to gaseous emboli (13%) occurred during wire and pigtail manipulation. Perera et al[25] demonstrated a reduction in the number of HITSs with robotic catheter placement, and this technique could be explored to reduce embolization in this phase. The increase in DW-MRI lesion surface area ($r_s = 0.928$; $P = .01$) with an increased number of solid HITSs (Fig 3, *C*), the association between a more diseased aortic arch and increased MRI lesion diameter (≥3 mm; Fig 3, *B*), and the presence of embolic material captured within the filters, all support the hypothesis that solid particle embolization contributes to brain injury.

Emboli differentiation in the present study has characterized a significant proportion of the total HITSs observed as gaseous (91%), with 9% considered solid. This should be interpreted with caution, because all the patients received embolic protection and capture of debris could have underestimated the true proportion of solid embolization. The sensitivity and specificity for emboli differentiation with the dual-frequency TCD software has been reported to vary (50.3% and 96.5%).[26] In the present study, we accounted for this by machine count and independent analysis of each embolus by two trained specialists to reduce error. Nevertheless, our findings are in keeping with those from emboli differentiation studies for other interventional procedures, which demonstrated a high proportion of gaseous embolization during procedures such as carotid endarterectomy, carotid artery stenting,[23] coronary catheterization,[22] and cardiac surgery.[24]

An increase in the number of gaseous HITSs was associated with an increased number of DW-MRI lesions ($r = 0.912$; $P = .01$) but had no effect on lesion surface

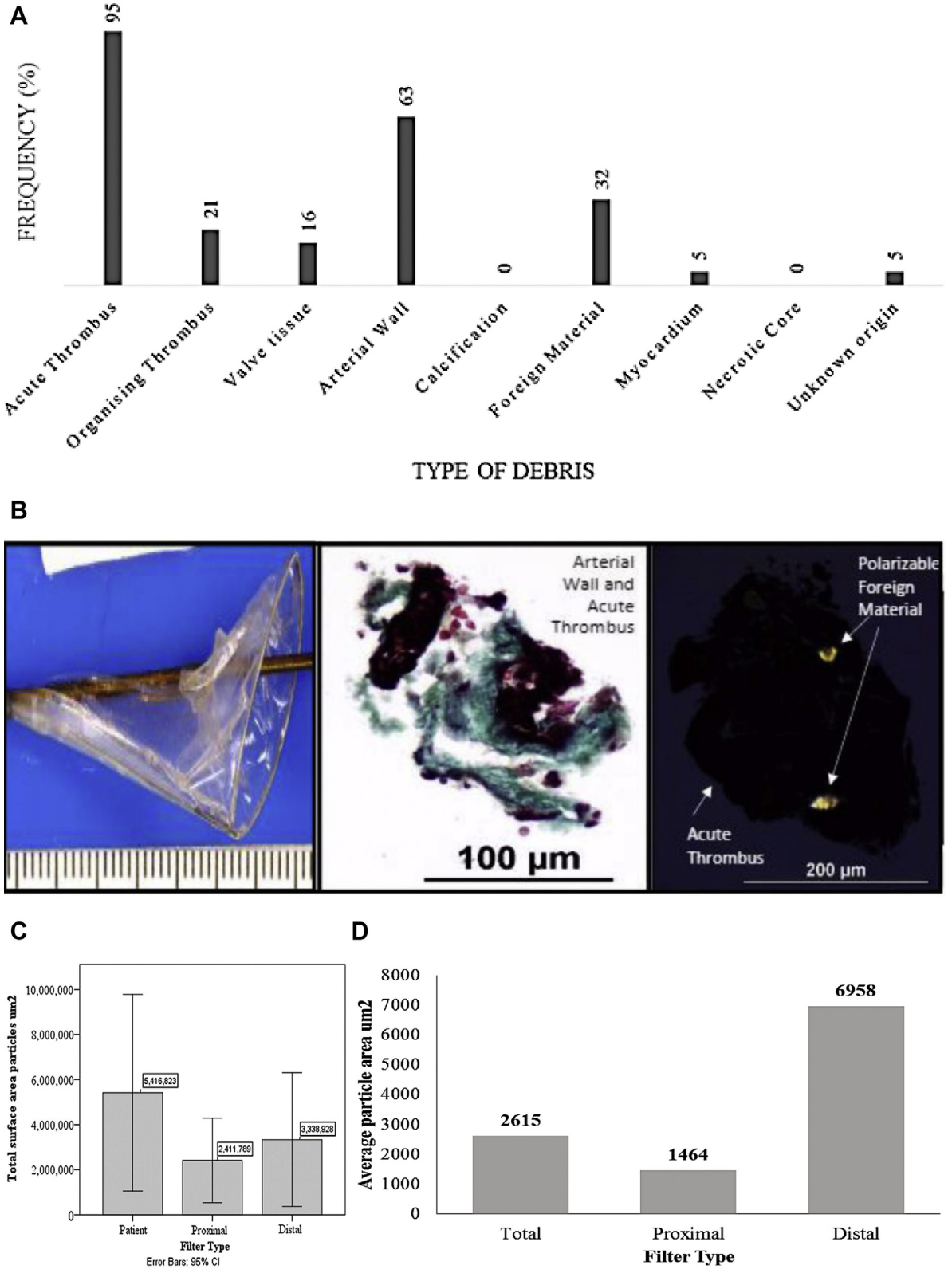

Fig 5. A, Frequency of types of debris. **B,** Most commonly found debris. **C,** Total surface area of particles per filter. **D,** Average particle surface area per filter.

area. Although gaseous emboli are smaller (4 μm) and thought to diffuse in blood, the cumulative effect of large numbers of gaseous emboli can contribute to ischemic injury and have been linked with neurocognitive decline after cardiac surgery. The use of gas filters has shown a trend toward improved cognitive outcomes.[24]

Embolic showers in TEVAR (Fig 2, *B*) could be explained by the presence of "trapped gas" in the endografts, which is released into the cerebral circulation during stent deployment. A recent in vitro study demonstrated that ≤0.04 mL of air is released from the Gore c-TAG and 0.3 mL from the Medtronic Valiant with visualized bubbles of ≤3 mm.[27] Mechanisms to reduce gaseous embolization have been proposed such as the flushing of the stents with carbon dioxide.[28] The proximity to the arch vessels, temporary loss of antegrade flow, and cerebral hypoperfusion could all contribute to the passage of bubbles into the intracranial circulation.

Study limitations. The current generation of the Sentinel CPS protects only two of the three supra-aortic trunks. The left vertebral artery remains unprotected and therefore, the left PC is most vulnerable to embolization, representing a limitation of the device. It is unsurprising that most new infarcts were in the cerebral territories served by the PC. Lesions in both the left and the right PC (39% and 26%), with most in the cerebellum, are shown in Fig 4. The lesions in the right PC can be explained by the passage of emboli through the unprotected left vertebral artery, by way of the posterior communicating artery through an intact circle of Willis.

The present pilot study used the device in TEVAR with landing zones distal to the left subclavian artery (zones 2-4) with deployment of both filters (Fig 1, *B*). It has been well recognized that the greatest rates of stroke are observed with stenting in the aortic arch more proximally (landing zones 0 and 1).[3,4] In theory, deployment of only the proximal filter in the brachiocephalic trunk after carotid-carotid bypass for cerebral revascularization before stenting across zone 1 and deployment of a proximal filter in a suitable diameter (range, 9-15 mm) neoinnominate artery for zone 0 TEVAR could hypothetically protect the brain in these more proximal high-risk landing zones.

The present feasibility study was limited by small patient numbers; therefore, we did not seek to provide a definitive answer regarding whether the use of the CEPD prevents stroke in patients undergoing TEVAR. The study has nonetheless identified a significant proportion of gaseous and solid embolization during TEVAR. In addition, the rate of embolization during device placement itself must be considered.

CONCLUSIONS

Stroke remains a sequela of TEVAR, with concern of high rates of SCI and subsequent neurologic deterioration. These initial cases suggest that the Sentinel CPS is safe to use in TEVAR, including in the emergency setting. The CEPD could serve as a useful adjunct, with a high rate of embolic debris capture and an overall reduction in the size of MRI-detected cerebral injury compared with historical neuroimaging data. A randomized controlled trial or anatomically matched cohort would provide further insight on the absolute cerebral infarction reduction.

The identification of a significant proportion of gaseous embolization, and its role and contribution to cerebral injury requires further investigation. Ultimately, a technique aimed at both solid and gaseous embolic protection in a randomized controlled setting is desirable to reduce the incidence of brain injury in TEVAR.

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AUTHOR CONTRIBUTIONS

Conception and design: GG, AP, NR, AD, RG
Analysis and interpretation: GG, CB, AS, AD, RG
Data collection: GG, AP, MH
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Final approval of the article: GG, AP, NR, MH, CB, AS, AD, RG
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