A percutaneous aortic device for cerebral embolic protection during cardiovascular intervention

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Background: Embolic stroke is a major cause of morbidity in aortic and cardiac interventional procedures. Although cerebral embolic protection devices have been developed for carotid interventions and for open heart surgery, a percutaneous device for cerebral embolic protection during aortic and cardiac interventions would be desirable.

Methods: The Embrella Embolic Deflector (Embrella Cardiovascular Inc, Wayne, Pa) is a percutaneously placed embolic protection device, inserted by a 6F access in the pig’s right forelimb, and deployed in the aorta, covering the brachiocephalic vessel origins. The device functions by deflecting embolic debris downstream in the aortic circulation. A swine model (n = 3) was developed for testing the deployment, retrieval, and efficacy of the device using a carotid filtration circuit for collection of emboli. Human atheromatous material was prepared as embolization particles with diameters between 150 and 600 μm. Deflection efficiency of the device was calculated by comparing numbers of embolic particles in the carotid circulation during protected and unprotected injections.

Results: The device was reliably deployed, positioned, and retrieved (n = 24). There was no significant drop in blood pressure across the membrane of the device to suggest reduction of cerebral blood flow. The device did not become occluded by embolic debris despite an embolic load many times that encountered in the clinical situation. Particles entering the carotid circulation after aortic injection of emboli were reduced from 19% of total (unprotected) to 1.3% (protected, P < .0001), with 98.7% of all injected particles being deflected downstream. There was no evidence of arterial injury related to the device found at necropsy.

Conclusion: The Embrella Embolic Deflector performs safely and reliably in the swine model of human atheroembolism. It effectively deflects almost all emboli downstream, away from the carotid circulation. The deflector shows promise as an aortic embolic protection device and merits further investigation. (J Vasc Surg 2011;54:174-81.)

Clinical Relevance: Embolic stroke plagues cardiovascular interventions involving manipulation of the heart and proximal aorta. An embolic protection device for use during these interventions which can be percutaneously placed is desirable in order to reduce the cerebrovascular risk of these interventions.

The Embrella Embolic Deflector (Embrella Cardiovascular Inc, Wayne, Pa) was designed to meet the need for embolic protection during procedures on the heart or involving the passage of catheters over the aortic arch. Emboli may arise from manipulation of the heart valves or atria in addition to the aortic surface. The need for protection from these embolic events has become more acute because these procedures have become more frequent and endovascular solutions are being devised and used for an ever-increasing number and variety of cardiac and vascular problems. In this setting, unlike that of open surgery, there is no opportunity to “wash out” or “flush” emboli, resulting in serious neurologic events that range from life-threatening strokes to “asymptomatic infarcts,” lesions found on diffusion-weighted magnetic resonance imaging with no apparent clinical correlate. Procedures that involve manipulating catheters around the vicinities of the aortic root, particularly in the setting of significant atherosclerotic disease, would benefit from protection against carotid emboli.

Even small catheters used for cardiac catheterization have been shown to scrape debris off the aortic arch and have an associated risk of emboli to the brain. One study showed that in 1000 consecutive percutaneous cardiac revascularization procedures, the guiding catheter had scraped debris from the aorta in >50%. A recent animal study showed that emboli are
generated by passage of catheters across even a noncalcified aorta. A clinical study showed cerebral emboli were detected in 100% of patients undergoing cardiac catheterization by transcranial Doppler, although all patients were asymptomatic. One notable study of 101 patients with aortic stenosis who underwent retrograde catheterization of the aortic valve showed focal diffusion-imaging abnormalities after the procedure in a pattern consistent with acute cerebral embolic events in 22% of patients, and 3 (3%) had clinically apparent neurologic deficits.

Balloon aortic valvuloplasty (BAV) has become more prevalent and is now used as a step before placement of percutaneous valves and as a palliative measure for patients who are not candidates for transcatheter aortic valve implantation (TAVI). Valvuloplasty involves passage of large catheters across the aortic arch, as well as balloon fracture and manipulation of sclerotic aortic valves. Thoracic endovascular aortic repair (TEVAR) also involves the passage of large catheters through the aortic arch, and embolic strokes have been seen in an average of 2.9% of cases, with a range of 0% to 19% in different studies according the definition. The stroke rate for TEVAR increased dramatically to 27.7% when the thoracic aorta repair extended up to the level of the proximal descending aorta. A study involving passage of large catheters through the brachiocephalic artery ostium showed a risk of emboli correlated with a finding of mobile emboli as well as to the location and extent of atherosclerotic disease in the ascending aorta. Percutaneous aortic valve replacement involves manipulation of the aorta and the aortic valve in patients at risk for atheroma. Risk of emboli correlated with a finding of mobile emboli as well as to the location and extent of atherosclerotic disease in the ascending aorta. Stroke rates for TAVI are between 4% and 11%.

The major risk of emboli is that they will enter the brain. Downstream end organs have redundant blood supplies and can tolerate emboli of a size that would cause stroke or even death in the cerebral circulation. Presently, cardiac catheterization, percutaneous interventions, BAV, TAVI, and TEVAR are all performed without embolic protection, with the risk of cerebral emboli considered unavoidable and the risk of other downstream emboli considered acceptable. Embolic protection devices currently in use, which are able to protect both carotid arteries from embolic material, span the entire aortic lumen, such as the Embol-X device (Embol-X, Inc, Mountain View, Calif). Used only in open cardiac procedures, this device collected particulate matter in 97% of cases.

METHODS

Device. The Embrella Embolic Deflector (Fig 1) cerebral embolic protection device consists of a nitinol frame and porous membrane with 100-μm pores that allow continuous blood flow through the device while deflecting embolic debris. The deployed device covers the ostia of the innominate and left common carotid arteries, deflecting debris downstream in the aorta. It is inserted percutaneously through a 6F sheath placed in the right forelimb.

Animal model. Three female or castrated Domestic Yorkshire swine (Sus scrofa) weighing 56 to 63 kg were used for the experiments, performed under good laboratory practice protocol. One intramuscular muscarinic anticholinergic dose (glycopyrrolate, concentration 0.2 mg/mL; dosage, 0.005-0.02 mg/kg) was given before the preprocedure. Induction was achieved with a rapid acting general anesthetic consisting of tiletamine and zolazepam (Telazol [Fort Dodge Animal Health, Fort Dodge, Iowa]; concentration, 100 mg/mL; dosage, 2.5 mg/kg). Animals underwent endotracheal intubation and were maintained with 1% to 3% of continuous inhalation of isoflurane. As an acute procedure, analgesics and antibiotics were not indicated as part of the protocol. The animals were heparinized with 5000 to 10,000 U intravenous bolus to maintain an activated
clotting time >300 seconds and had been pretreated with aspirin (650 mg) and clopidogrel (300 mg) 1 day before the procedure and aspirin (325 mg) and clopidogrel (150 mg) on the day of the procedure.

The left and right carotid arteries and the right jugular vein were surgically exposed and cannulated with 10F arterial perfusion cannulae (Edwards Lifesciences, Irvine, Calif; Fig 2). A circuit was created that routed the blood flow through silicone tubing from each carotid through a cartridge containing a changeable 78-μm pore filtration disk (Fig 3) and returned that blood to the jugular vein. Thus, all carotid blood flow passed through the filtration system.

For purposes of blood pressure monitoring and arteriography, a 6F sheath (Terumo Inc, Ann Arbor, Mich) was percutaneously placed in the right femoral artery. A 6F hydrophilically coated sheath (Cook Inc, Bloomington, Ind) was percutaneously inserted into the right forelimb artery using a Seldinger technique with its tip positioned at the ostium of the innominate artery. Arterial pressure measurements were simultaneously recorded from the innominate and femoral sheaths.

An aortogram was performed with a calibrated pigtail catheter (Angiodynamics Inc, Queensbury, NY) to measure aortic dimensions and view branching anatomy of the great vessels (Fig 4).

The Embrella Embolic Deflector was inserted via the 6F forelimb sheath, which had been inserted over a wire and positioned at the ostium of the innominate artery. Then, the device was pushed out into the aorta allowing the device to self-expand. The device was deployed under fluoroscopic guidance (Fig 5, online only) and was secured into position covering the ostia of both the innominate and left common carotid arteries. Positioning was confirmed by contrast injection of the forelimb sheath, demonstrating that the device was seated along the greater curvature of the aortic arch covering the ostia of the innominate and left common carotid arteries. The sheath was maintained in the innominate artery for removal after the device had been retrieved back into it. The device was retrieved by withdrawing it into the forelimb sheath and then removing it.

At the conclusion of the experiments, the animal was euthanized by injection of potassium chloride and the aorta examined for evidence of injury (Fig 6).

**Embolization.** Human atheromata derived from cadaver aortas was harvested. Atherosclerotic material was cut into pieces and ground in a standard tissue homogenizer. The resulting material was filtered using several certified laboratory sieves resulting in emboli sizes ranging from 150 to 300 μm (stained with blue tissue marking dye) and 300 to 600 μm (stained with orange tissue marking dye). The resulting particles were suspended in saline, and an aliquot was studied, which revealed a particle concentration of 143 particles/mL (98 blue, 45 orange). A 4-mL aliquot of this solution was injected into the ascending aorta via a standard 6F pigtail catheter, positioned at the level of the aortic valve, and

Fig 3. A, The filters in the carotid shunt circuit are approximately the size of a dime, with one for each carotid (left and right). They collect all emboli passing through the carotid circulation. The emboli are made of human atheroma and are color coded by size; blue are 150-300 μm and orange are 300-600 μm. Filters collected emboli from (B) unprotected injections, (C) injections with the deflector device deployed, and (D) at the time of device retrieval.
followed by a flush of 30 mL of normal saline solution to clear all emboli from the catheter and tubing.

Emboli collected in the carotid filtration cartridges were counted under a dissecting microscope and recorded, as well as the number of emboli residing on the Embrella Embolic Deflector membrane upon retrieval. Carotid filtration cartridges (Fig 3) were removed for examination 15 seconds after injection of emboli either with (test, Fig 3, C) or without (control, Fig 3, B) the Embrella Embolic Deflector in place. The 15 seconds allowed for several cardiac cycles to eject all of the emboli out of the aortic arch. In addition, to determine how many emboli were shed during retrieval of the Embrella Embolic Deflector, the carotid filtration cartridges were examined again 15 seconds after the retrieval step (Fig 3, D). Control injections were performed before every test injection.

Statistics. The total number of downstream-deflected particles was determined to be equal to the total number of particles injected (Pi), (injection volume × particle concentration) less the sum of the number of particles captured in the carotid filtration system and retained on the device.

Deflection efficiency (DE) was determined by comparison of the number of particles captured by the carotid filters during an unprotected injection (Pc, control) to the number of particles captured by the carotid filters during protected injections (test). The total number of particles escaping the Embrella Embolic Deflector to enter the carotid arteries was determined as the sum of those noted in the filters after emboli injection with the device deployed (Pd) and after the retrieval step (Pr). Thus, carotid deflection efficiency (%) was calculated as: \[ \text{DE}_{\text{carotid}} = \left( 1 - \frac{(P_d + P_r)}{P_c} \right) \times 100. \]

Total deflection efficiency was also calculated, indicating the percent of total injected particles deflected downstream: \[ \text{DE}_{\text{total}} = \left( 1 - \frac{(P_d + P_r)}{P_i} \right) \times 100. \]

The t test was used for comparison of means.

RESULTS

We tested 24 devices in three animals weighing a mean 59 kg (range, 56-63 kg). The aortic arch diameters varied from 24.7 to 28.3 mm. The devices were successfully deployed and retrieved in every case and reliably covered the ostia of the innominate and left common carotid arteries upon initial deployment, without the
need for repositioning or manipulation as confirmed by contrast injection.

No significant pressure gradients (>5% mean arterial pressure difference between forelimb and femoral sheaths) were noted at any time across any of the deployed devices, as measured continuously by the femoral and innominate sheath transducers (Fig 7).

**Deflection studies.** A baseline aortic injection of embolic particles without the device in place resulted in 19% of particles (range, 15%-24%) traveling to the carotid circulation and 81% (range, 76%-85%) traveling downstream in the aortic circulation. With the device in place, the percentage of particles deflected downstream increased from a mean of 81% to 98.7% ($P = .0029$; Table). The overall DE for carotid emboli was 91.1% (range, 77.0%-100%). The average number of particles passing through the carotid filters was reduced from a baseline (unprotected) average of 110 to 8.7 particles when protected by the device ($P < .0001$). There was no

**Fig 7.** Femoral-forelimb pressure differential was measured continuously at the femoral and innominate sheath tips. The innominate sheath tip was on the distal side of flow across the Embrella embolic deflector. No significant pressure gradients across the device were observed.

**Table.** Deflection efficiency

<table>
<thead>
<tr>
<th>Animal</th>
<th>Devices</th>
<th>Injection type</th>
<th>Total carotid filters, No.</th>
<th>Device membrane retained, No.</th>
<th>Carotid</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1–8</td>
<td>Control</td>
<td>87 ± 14.6</td>
<td>56.6 ± 27.1</td>
<td>85.1 ± 5.9</td>
<td>97.7 ± 0.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deployed</td>
<td>7.0 ± 4.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrieved</td>
<td>6.0 ± 3.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>9–16</td>
<td>Control</td>
<td>140 ± 11.5</td>
<td>3.3 ± 2.3</td>
<td>97.9 ± 1.6</td>
<td>99.5 ± 3.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deployed</td>
<td>2.9 ± 2.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrieved</td>
<td>0.1 ± 0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>17–24</td>
<td>Control</td>
<td>103.4 ± 24.2</td>
<td></td>
<td>90.3 ± 6.7</td>
<td>98.3 ± 12.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deployed</td>
<td>7.4 ± 5.9</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Retrieved</td>
<td>2.6 ± 6.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>91.1 ± 7.3</td>
<td>98.5 ± 9.2</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

*Human atheromatous emboli were injected in the ascending aorta, with (deployed) and without (control) the Embrella embolic deflector in place, and collected in a carotid filtration circuit.*
significant difference in deflection efficiency between small (150-300 μm) and large (300-600 μm) particles.

The devices did not become overwhelmed or occluded by embolic load despite injections of large amounts of embolic material, as evidenced by the absence of any change in pressure gradient across the devices after injection. The porous membrane of the devices retained relatively few particles (mean, 23; range, 0-101), deflecting most particles downstream. The surface area of the deployed device was 10.84 cm², and the maximum surface area of adherent emboli was far less than 1% of the total device surface area.

Gross inspection of the aorta at necropsy revealed no signs of injury at the site of device deployment despite multiple deployments in most animals (Fig 6).

DISCUSSION

Aortic and cardiac interventional procedures are associated with a significant risk of embolic stroke. Transcatheter aortic valve procedures have a reported stroke rate of 4% to 11% and stroke represents the most prevalent major morbidity associated with this new technology. Thoracic endovascular aneurysm repair is also prevalent major morbidity associated with this new technology. These strokes are largely attributable to the dislodgement of emboli that enter the cerebrovascular circulation. A device that provides embolic protections during aortic and cardiac interventions would significantly enable the further development of these minimally invasive procedures.

The Embrella Embolic Deflector was easily deployed and retrieved using familiar techniques through a percutaneously placed 6F right arm sheath. The device was deployed within the aorta without significant interaction with the aortic walls. The device self-aligned in the aorta to cover the ostia of the brachiocephalic vessels. The positioning and sealing of the device were easily confirmed by contrast injection of the delivery sheath. Because the device enters the aorta through the right subclavian artery, it is “out of the way” of index procedures that will chiefly use femoral artery access routes to the aorta or heart. Its low profile against the greater curvature of the aorta allowed unimpeded passage of catheters and wires used in the study. The device performed reliably in deployment, sealing, and retrieval in all of our studies. Inspection of the aortas showed no evidence of injury after eight deployments and retrievals. The pigs in this study had nonatherosclerotic aortas, which is a limitation of the study.

Traditional distal embolic protection devices rely upon filters to capture emboli. A main difference with this technique is that it provides embolic protection by deflection rather than collection of emboli. Emboli ricochet off of the device towards downstream aortic beds, which are much more redundant and forgiving in their blood supply and branching patterns than the cerebrovascular circulation. In the case of a very large embolus capable of causing significant injury to a downstream organ, the effect would likely be less devastating than a stroke caused by the same embolus and the patient could potentially be treated with embolectomy. The 100-μm pores of the device exclude dangerous emboli yet permit brisk blood flow. The pore size was chosen based on the pore size of commercially available embolic protection devices, which have been shown to decrease the number of clinically dangerous emboli.

No significant pressure gradients across the membrane were noted when comparing femoral with innominate artery pressures. The device is continuously “purged” by the cardiac output washing the surface clean of emboli. At a maximum, <1% of the surface area was covered by emboli adherent to the membrane of the device despite the delivery of embolic loads many times greater than those encountered in the clinical situation. This feature offers a significant advantage over traditional cerebral protection devices with filter-capture protection schemes that can become occluded by trapped emboli limiting flow through to the brain.

The device diverted an average of 98.7% of the total delivered embolic load downstream, away from the carotid circulation. Looking specifically at the dangerous emboli destined for the carotid arteries, the deflection efficiency for carotid emboli was 91.1% compared with controls. The latter number compares the number of emboli noted in the carotid filters for an unprotected injection vs a protected injection. This compares favorably with other distal embolic protection devices. Several authors have performed in vitro testing of filter capture efficiency.

Siewiorek et al embolized resin microspheres in a flow model simulating the carotid circulation with carotid cerebral protection devices deployed. They found a capture efficiency of 95% for the FilterWire EZ (Boston Scientific, Natick Mass), 92% for the Accunet (Guidant Corp, Indianapolis, Ind), and 62% for the Emboshield (Abbott, Abbott Park, Ill).

Order et al, in a similar in vitro carotid model using microspheres, obtained capture efficiencies of 84% (TRAP; Microvena, White Bear Lake, Minn), 94% (FilterWire EX; Boston Scientific) and 70% (Angioguard; Cordis, Miami Lakes, Fla).

Rapp et al, in a carotid flow model of protected carotid angioplasty using intact excised human carotid endarterectomy specimens, found low capture efficiency for distal protection devices when confronted with human atheromatous emboli. Capture efficiencies ranging from only 13.7% to 28% were documented for the Spider (ev3 Endovascular, Inc, Plymouth, Minn), FilterWire EZ, Accunet, Angioguard, and Emboshield, suggesting that atheromatous emboli present a greater challenge than do microspheres. The observed “leak path” for these carotid embolic protection devices was around the sealing edge of the device where the wire frame circumferentially contacts the vessel wall. The pore size of the device could be changed if this were deemed clinically beneficial. Devices with pore sizes down to 40 μm allow adequate flow in the human bloodstream.
Although the deflection efficiency of the Embrella device was high, it was not perfect. Possibly some emboli pass around the sealing edge of the device rather than through its pores. The device seals by conforming its nitinol wire perimeter with the surface of the aorta. The pulsatile turbulent flow in the arch might allow an embolus to slip past the edge. The ability to seal well on an irregular surface in the presence of a diseased arch remains to be determined. Some emboli also entered the carotid circulation during the retrieval phase of the procedure. Suggested mechanisms might include release of emboli trapped between the sealing edge of the device and the aorta at the time of retrieval or shedding of emboli from the surface of the membrane during retrieval. The latter situation may be benefited by a “downstream” resheathing of the device.

The safety of the device was demonstrated by its reliable deployment and retrieval and absence of any gross evidence of vessel trauma at necropsy. Histologic examination in a future study will provide a more detailed analysis. In addition, the device did not significantly reduce cerebral blood flow while deployed.

The animal model proved useful for study of the device. Pigs weighing >50 kg had aortic dimensions comparable to humans. The branching anatomy of the porcine arch provides a single brachiocephalic vessel from which the left and right carotids and the right subclavian artery derive. The second arch vessel is a separate left subclavian artery. This two- vessel arch anatomy is seen in 15% of humans with the bovine arch variation. Measurement of blood pressure at the tip of the brachiocephalic sheath provides sampling of the entire carotid circulation due to the common origin of both carotid arteries. The human atheromatous embolism preparation provided for a more “realistic” challenge of physiologic irregularly shaped embolic material than would be possible with resin microspheres. These embolic particles performed reliably and reproducibly in our experiments and we believe they are an excellent surrogate for the clinical situation of plaque-related embolization during interventional procedures.

The carotid shunt circuit provided high flow reliably. Initial attempts to route flow from each carotid through the filtration circuit and back to the distal ipsilateral carotid failed to provide adequate flow due to intractable vaso- spasm in the distal carotids. By returning blood flow to the jugular vein, a reliable shunt circuit was established with high flow. Of the embolic particles injected during control experiments, 19% entered the carotid circulation with this shunt circuit in place, which is consistent with a physiologic distribution of cerebral blood flow as a percentage of cardiac output.

CONCLUSIONS

The Embrella Embolic Deflector performs safely and reliably in a swine model of aortic embolization of atheromatous debris. It deflects 98.7% of aortic emboli downstream, away from the carotid circulation. It does not impede cerebral blood flow or become overwhelmed by adherent emboli, nor does it cause apparent injury to the aorta. Further investigation of the device and its applications to interventional aortic and cardiac procedures is warranted.

AUTHOR CONTRIBUTIONS

Conception and design: JPC, JTC, JG, AT
Analysis and interpretation: JPC, JTC, JG, AT, AT
Data collection: JPC, JTC, JG, JW, GH
Writing the article: JPC, JTC, JG, JW, AT
Critical revision of the article: JPC, JTC
Final approval of the article: JPC, JTC, JG, JW, AT
Statistical analysis: JPC, JTC
Obtained funding: JPC, JTC, JW, JG, AT, GH

Overall responsibility: JPC

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Fig 5. (online only). A, Fluoroscopic appearance of the deployed Embrella Embolic Deflector. The pigtail catheter is positioned for emboli injection. B, Injection of the brachiocephalic via the forelimb sheath reveals a “seal” behind the device, and opacifies the innominate and left subclavian arteries.