Embolic protection devices

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Percutaneous intervention for the treatment of coronary and peripheral atherosclerotic disease has become a well established technique, and has been recently extended also to the carotid arena. However, distal embolisation of particulate matter, including plaque debris such as fibrin, necrotic atheromatous core, foam cells, cholesterol clefts, and thrombus,¹ at the time of balloon inflation or stent deployment, complicate percutaneous mechanical interventions more often than had been recognised before. The risk of distal embolisation is now considered significant in carotid arteries,² degenerated saphenous vein graft, and in thrombotic lesions characterising the patient affected by acute coronary syndromes.³⁻⁵ The process of plaque embolisation catalyses a complex interaction also involving microvascular spasm and thrombosis. This often results in diminished blood flow to the distal vascular bed, potentially complicated by periprocedural ischaemia and/or infarction or stroke.^{6,7} In particular, the risk of distal embolisation is especially high in degenerated saphenous vein grafts, with the "no reflow" phenomenon being reported in up to 31.8% of cases during treatment of thrombotic lesions and in up to 7.9% of cases with no thrombus present.⁸ Although large particles (> 100 µm) may obstruct large, epicardial vessels, very small particles, as little as 15-50 µm, can also obstruct the microvascular bed causing microinfarcts and left ventricular dysfunction. In the setting of acute myocardial infarction, Ito and associates⁹ detected by myocardial contrast echocardiography a substantial "no reflow" area, potentially related to distal embolisation of atherosclerotic debris in 37% of patients with TIMI-3 flow shortly after reperfusion treatment. Those "infarctlets", indicated by an increase in periprocedural creatine kinase-MB, have been recently associated with worse outcome at one year follow up, even in patients without any apparent procedure or in-hospital complications.¹⁰

Different approaches have been attempted in the past to reduce distal embolisation, including intracoronary administration of urokinase,¹¹ extraction coronary atherectomy,¹² directional coronary atherectomy,¹³ laser angioplasty,¹⁴ ultrasound thrombolysis,¹⁵ and AngioJet rapid thrombectomy.^{16,17} The results, however, were not considered to be satisfactory in terms of achieving a significant reduction in distal embolisation.

Over the last few years, several distal protection devices have been introduced to allow the capture and retrieval of friable, lipid-rich plaque constituents released after percutaneous interventional procedures, before they lodge in the distal microcirculation. Currently available technologies for embolic protections have focused either on conduit occlusion (proximal or distal) with subsequent aspiration or on distal filter capture debris (table 1).

BALLOON OCCLUSION DEVICES

The PercuSurge GuardWire, the device with the most clinical use, is a temporary distal occlusion system that comprises three components: (1) the GuardWire temporary occlusion catheter containing a central lumen connected to a low pressure distal occlusion elastomeric balloon incorporated into the

tip and with a diameter ranging from 3-6 mm—the low profile of the deflated balloon facilitates lesion crossing providing protection from distal embolisation; (2) the MicroSeal adapter that controls the opening and closure of a proximal valve in the GuardWire, allowing inflation and deflation of the distal occlusion balloon; and (3) the Export aspiration catheter that consists of a 5 French monorail catheter connected to an evacuated 20 ml syringe used to remove thrombotic debris—after that, the GuardWire balloon is deflated and the anterograde flow is restored. One of the most important limitations of this distal balloon occlusion device is that it may cause distal ischaemia that may not be tolerated by some patients. In addition, filter preparation is cumbersome and angiography cannot be performed while the distal balloon is inflated, making assessment of the artery and stent placement more difficult.

Preliminary encouraging results with the PercuSurge GuardWire¹⁸ have been confirmed in the SAFER (saphenous vein graft angioplasty free of emboli randomized) trial conducted in the USA at 47 sites.¹⁹ The trial randomly allocated 406 patients to stenting with embolic protection and 396 patients to standard care without embolic protection during vein graft percutaneous coronary intervention. The primary end point, a composite of death, myocardial infarction, emergency bypass or target lesion revascularisation at 30 days, was significantly reduced in the group of patients assigned to treatment with the protection device compared to patients assigned to standard care (9.6% v 16.5%). This 42% relative reduction in major adverse cardiac events (MACE) was driven by reductions in myocardial infarction (8.6% v 14.7%) and no reflow phenomenon (3% v 9%). Interestingly, although adjunctive prophylactic treatment was administered (non-randomized allocation) to ≥ 60% of patients enrolled in the trial, a similar magnitude of MACE reduction was provided by mechanical embolic protection whether glycoprotein IIb/IIIa inhibition was administered (18.1% to 10.8%) or not (14.1% to 8.0%), attesting to the diverse pathogenesis of atheroembolism and the prominent importance of mechanical microvascular obstruction. Similarly, the feasibility and safety of carotid angioplasty using the PercuSurge system has been determined in different series such as the CAFÉ USA and the SHELTER registries with different success and complications rate.^{20,21}

FILTER DEVICES

The AngioGuard device consists of an angioplasty guide wire with an expandable porous filter at the distal tip. The filter is made of a thin, porous polymeric membrane supported by a fine metal skeleton. After crossing the lesion and reaching the

Abbreviations: CEA, carotid endarterectomy; GUARD, saphenous vein graft intervention using AngioGuard for reduction of distal embolization; MACE, major adverse cardiac events; SAFER, saphenous vein graft angioplasty free of emboli randomized; SAPHIRE, study of angioplasty with protection in patients at high risk for endarterectomy; TIMI, thrombolysis in myocardial infarction

Table 1 Distal protection devices currently available or under development

Device type	Device name	System components	Manufacturer	Material	Guidewire	Pore size	Guide compatibility	Indication
Proximal occlusion	Arteri-A-Parodi	PEAC balloon catheter, ECA occlusion balloon, arterial-venous shunt w/filter	Arteria Inc	PTFE/PU	0.035 inch	NA	10 French	Carotid
	MO. MA	PEAC balloon catheter, ECA occlusion balloon, arterial-venous shunt w/filter	Invatec		0.035 inch	NA	9–11 French	Carotid
Distal occlusion	GuardWire (MDT-Percusurge)	Guardwire (wire + balloon), Medtronic inflation device, Export aspiration catheter		Hollow Hypotube	0.014 inch 0.018 inch	N/A	8 French	Peripheral, carotid, coronary
Filter device	AngioGuard XP	Filter, deployment sheath, capture sheath, torque device	Cordis	PU/Nitinol	0.014 inch	100 µm	8 French	Peripheral, carotid, coronary
	Bsc-FilterWire EX	Delivery catheter, filter, capture sheath	Embolic protection	Nitinol	0.014 inch	80 µm	4 French	Carotid, coronary
	AccUNET	Delivery catheter, filter, capture sheath	Guidant	PU/Nitinol	0.014 inch	120 µm		Carotid, coronary
	Mednova, Neuroshield	Delivery catheter, filter, capture sheath	Abbott	PU/Nitinol	0.014 inch 0.018 inch	150 µm	9 French	Peripheral, carotid, coronary
	Mednova MDT-Filter	Delivery catheter, filter	Medtronic	Nitinol	0.014 inch	100 µm	7 French	Peripheral, coronary
	E-Trap/E-Sack	Delivery catheter, filter, capture sheath	Metamorphic	Nitinol	0.014 inch	100 µm	6 French	Peripheral, coronary
	TRAP	Delivery catheter, filter, capture sheath	Microvena	Nitinol wire, woven basket	0.014 inch		6 French	Peripheral
	Sulzer-IntraGuard	Delivery catheter, filter, capture sheath	IntraTherapeutics	Nitinol	0.014 inch	100 µm	6 French	Peripheral

distal site, the filter is expanded and routine angioplasty is performed. As the blood passes through the filter, emboli are captured in the filter. At the end of the procedure, the filter is collapsed, trapping embolic debris, which are retrieved by retracting the wire into a retrieving catheter. As opposed to the balloon occlusion device that produces complete interruption of antegrade flow and does not allow perfusion during the procedure, the AngioGuard ensures normal blood flow continuously. Practical advantages of this filter include its ease of use, good visibility, and crossing profile. A disadvantage is represented by a fairly stiff retrieval pod with potential difficulties in crossing the stent during filter withdrawal. At present, the AngioGuard filter device is still under investigation in the USA for both coronary and carotid percutaneous interventions. In particular, the SAPPHIRE (study of angioplasty with protection in patients at high risk for endarterectomy) trial has been designed to determine the benefits of stenting with the AngioGuard device compared to surgical carotid endarterectomy (CEA)²² in symptomatic patients with carotid stenosis $\geq 50\%$ and asymptomatic patients with carotid stenosis $\geq 80\%$. Preliminary results showed that 30 days MACE (death/stroke/acute myocardial infarction) was significantly lower in the stent group compared to the CEA group (5.8% v 12.6%, $p < 0.004$). The GUARD (saphenous vein graft intervention using AngioGuard for reduction of distal embolization) trial is still ongoing and will evaluate the efficacy of this device in a study population of 800 patients submitted for percutaneous coronary intervention.

The FilterWire EX (Boston Scientific, Natick, Massachusetts, USA) is a low profile (< 3.5 French) “fish-mouth” opening distal polyurethane filter with 80 µm diameter pore holes mounted on a 0.014 inch steerable angioplasty wire via a “spinner tube” which permits independent 360° rotation and steering of the wire. Pores allow antegrade blood flow while providing distal protection. The filter is attached to a radiopaque nitinol loop that is self expandable, allowing for complete contact of the filter against the arterial wall and

facilitating fluoroscopic visualisation. The collapsed filter (3.9 French crossing profile) is placed distal to the lesion and deployed by retracting the delivery sheath. The filter is then closed with the delivery/retrieval sheath after the procedure and withdrawn. Initial reports regarding feasibility, safety, and clinical efficacy are promising. Stone and associates²³ have reported a large multicentre experience with this device in a sequential two phase investigation conducted on 308 lesions in 278 saphenous vein grafts. Use of this device resulted in a low rate of periprocedural adverse events compared to historical controls (30 day rates of MACE occurred in 21.3% of patients in phase I, which was reduced to 11.3% in phase II, despite nearly identical patient and vein graft characteristics). This reduction was mainly caused by a decrease in Q wave and non-Q wave myocardial infarction. More recently, Grube and collaborators²⁴ have reported their experience with the FilterWire EX device in 35 consecutive patients undergoing elective carotid stenting at six centres. The FilterWire was delivered and deployed successfully in all cases, embolic debris was retrieved from 74% of procedures, and the 30 day rate of MACE (death, major or minor stroke) was 0%.

The MedNova NeuroShield (MedNova Inc, Galway, Ireland) consists of a 0.014 inch guidewire with a polyurethane filter mounted at the distal end. The system requires both a delivery and a retrieval catheter that in the latest generation are shorter and more flexible. Two large holes at the proximal end of the filter allow emboli to enter. The filter contains a pre-shaped nitinol expansion system that facilitates fluoroscopic visualisation, accurate deployment, and wall apposition. The filter guidewire is placed within the delivery catheter and is passed through the target lesion, the delivery catheter is withdrawn, the filter is deployed and, at the end of the interventional procedure, the retrieval catheter is used to envelop the filter. At this point, the entire device and its embolic contents are retracted.

CATHETER OCCLUSION DEVICES

The Parodi Anti-Emboli System (PAES; Arteria Medical Science, Inc, San Francisco, California, USA) and the MO.MA system are guiding catheters with a proximal occlusion balloon attached at the distal end. Both devices provide protection by reversing blood flow from the internal carotid artery into the sheath by means of negative pressure gradient through the guiding catheter. The external carotid artery is also occluded to avoid flow travelling from the external one back up the internal one. Although this elegant technique allows protection before the lesion is crossed and it can be used also in tight and tortuous vessels, the systems are bulky (11 French sheaths and 10 French guiding catheter are required) and there is a potential for damage of the artery at the site of balloon inflation. However, several cases have been reported with 100% successful deployment and no ipsilateral embolic events. The results of an ongoing European registry with the MO.MA device are shortly awaited.

LIMITATIONS

In general, each system has its own intrinsic limitations, and protection provided by these devices is far from "complete".²⁵ Causes of incomplete embolic protection include device crossing profile (larger profiles may lead to embolisation), incomplete filter apposition or conduit occlusion (especially in bending segments of the vessel), lack of protection of secondary branches, incomplete aspiration, filter pore size (either too large or small), device mediated vessel wall trauma, side branches ("backwash" during occlusion versus siphoning of debris during filter), and delayed platelet-white cell embolisation from the target site. In addition, balloon occlusion-type devices may cause distal ischaemia that may not be tolerated by some patients, and an aspiration catheter may not retrieve all the particles trapped in the artery. Finally, filter devices have a finite lower limit in the size of particles that can be captured and smaller particles can still get through the filter. A novel approach currently under evaluation that may circumvent many of these limitations involves proximal conduit occlusion (without crossing the lesion) and pressure driven aspiration from a catheter to evacuate particulate debris irrespective of particle size. This device (Proxis, Velocimed) also permits distal administration of drugs, such as vasodilators or cardioplegic or nutrient solutions, thus providing a double, pharmacomechanical approach to address the complex pathophysiologic process of embolisation.

CONCLUSION

Although several technical development and material improvements have been made in the construction of the distal protection devices, future iterative engineering is required to obtain an atraumatic system, with very low profile, high torqueability, and an ability to capture all of the plaque debris. Ultimately, only when the clinical efficacy of these devices has been clearly demonstrated in large clinical trials, involving patients with different risk profiles, will embolic protection systems be ultimately incorporated into the daily practice of percutaneous coronary and peripheral interventions.

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