Emboli protection devices in cardiovascular medicine

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Summary

Emboli protection devices (EPD) have a solid stand in the modern armamentarium of the interventionalist. However, the use of these devices is associated with a broad range of benefits in different cardiovascular territories. The most compelling data for mechanical emboli protection are available for percutaneous interventions of aortocoronary bypass grafts. In this setting, randomised studies have shown that the use of EPD is associated with a significant reduction in major adverse events. Nevertheless, current registry data suggest that the devices are used only in a minority of those cases. Conversely, in acute myocardial infarction, the routine use of EPD was not found to be beneficial. A strong consensus, though not unanimous, supports the use of these devices for carotid artery stenting. With respect to renal stenting, the experience is still at an early stage and the use of EPD cannot be recommended.

Key words: emboli protection devices; bypass grafts; percutaneous coronary intervention; carotid artery stenting

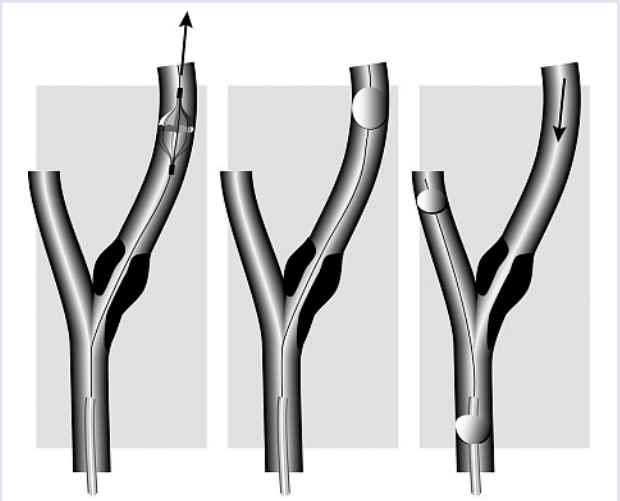
Introduction

Distal embolisation of plaque or thrombotic material may occur spontaneously during the process of plaque rupture and subsequent thrombus formation or may be induced by balloon angioplasty or stenting. The detection of this phenomenon, more frequent than previously believed, has been made possible by imaging technologies such as magnetic resonance, myocardial contrast echocardiography, and transcranial Doppler. The linkage between microvascular obstruction and unfavorable long-term clinical outcomes has been established for multiple vascular beds. Distal embolisation during percutaneous revascularisation may be prevented using a pharmacological (i.e., by periprocedural potent platelet inhibition and/or anticoagulation) or a mechanical approach.

The concept of mechanical emboli protection is based on the placement of a filter device between the lesion treated and the distal vasculature or by a blockage of the blood flow in the vessel – either proximally or distally to the lesion – followed by an aspiration of the blood column prior to allow flow. The different approaches of mechanical emboli protection, in the example of carotid artery stenting, are demonstrated in figure 1. As a general rule, filter-based emboli protection devices (EPD) are easy to use, allow blood flow throughout the procedure but particles smaller than the pore size (usually 100–150 μm) may reach the distal vasculature. Distal and proximal balloon occlusive devices allow for more complete re-

There is no conflict of interest.

Figure 1
Strategies for emboli protection devices in carotid artery stenting. On the left panel is demonstrated a filter device, in the middle a distal balloon occlusive device and in the right panel a proximal occlusive device. (Reproduced from [24]: Roffi M, Mukherjee D. Carotid artery disease management. In: Manual of Vascular Diseases. First edition. Ed. Rajagopalan S, Mohler E, Mukherjee D, editors. New York: Lippincott William and Wilkins; 2005. With kind permission, Copyright© 2009, Lippincott Williams & Wilkins, Baltimore, USA.)



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trieval of small particles suspended in the blood column at the time of intervention. The disadvantage of these approaches is the potential for ischaemia and the poor visualisation of the lesion (table 1). Protection devices have been tested – with different degree of success – in various arterial beds including the coronary circulation, aortocoronary bypass grafts, the carotid artery, and the renal artery. The purpose of this manuscript is to briefly review the data supporting the use of EPD in cardiovascular interventions.

Acute myocardial infarction

Several small studies have addressed the impact of EPD in the setting of acute myocardial infraction (MI). The largest of them was the EMERALD trial, which randomised 501 patients to conventional treatment or distal balloon protection. No difference was observed in terms of postprocedural ST-segment resolution on ECG, infarct size, or major clinical events at six months [1]. In a meta-analysis of eight randomised studies, for a total of 1467 patients, no difference in terms of postprocedural blood flow normalisation among patients with acute MI treated with protection and those without protection was observed [2]. However, an improvement in myocardial blush grade, suggesting a reduced damage of the microcirculation could be detected. Similarly, in the group treated with protection there was less frequently angiographic evidence of distal embolisation. Nevertheless, these findings were not associated with a survival benefit. In acute MI, the mainstay of distal embolisation prevention is a pharmacologic one based specifically on glycoprotein IIb/IIIa receptor (GP IIb/IIIa) inhibitors. Accordingly, the use of these agents has been associated with improved outcomes in this setting [3]. Adjunctive mechanical emboli protection should be reserved for selected cases with large thrombus burden (fig. 2).

Aortocoronary bypass grafts interventions

Percutaneous coronary intervention (PCI) of saphenous vein grafts (SVG) has been associated with less favorable outcomes compared to procedures involving the

Table 1
Pros and cons of emboli protection devices (after [23]).

Device type	Pros	Cons
Filter EPD	Preserve antegrade flow throughout the procedure	May not capture debris smaller than pore size
	Optimal visualisation of the lesion	Not as steerable as coronary wires[1]
	Lesion crossing with guide wire of choice possible (with wire-independent systems)	May cause spasm or dissection of the internal carotid artery
	Can be deployed and captured rapidly	Lesion crossing not protected
	Easy to use	Filter may cause flow obstruction (slow flow, no flow)
		Due to the stiffness of the device, may not be placed in the presence of excessive tortuousity
		Apposition in tortuous vessel may be suboptimal
		Transient flow obstruction may be poorly tolerated[2]
Proximal balloon occlusion ± flow reversal	All the steps of the procedures protected	
	Crossing of the lesion with guide wire of choice	Poor visualisation of the lesion
	Protection possible also in the presence of excessive tortuousity of the internal carotid artery	Handling more demanding
	Protection independent of particle size	Larger sheath size required
		Occlusive balloons may cause dissection or spasm of the common or external carotid artery
		Time consuming set-up
Distal balloon occlusion	Protection independent of particle size	Transient flow obstruction may be poorly tolerated[2]
	Lower profile and less stiff than filter EPD	Poor visualisation of the lesion
	More easily delivered in tortuous anatomy	Crossing of the lesion not protected
		Use more cumbersome
		Potential for balloon-induced injury
		Less steerable than coronary guide wire

[1] Does not apply for wire-independent systems.
[2] Problematic in patients with severe stenosis or occlusion of the contralateral internal carotid artery as well as in patients with isolated hemisphere.
EPD = emboli protection devices.

native coronary circulation. Acute complications include distal embolisation, "no-reflow", and higher rate of periprocedural MI. Vein graft and coronary atherosclerosis are to be considered different diseases. Graft atheroma is diffuse, friable, soft, and lipid-rich. The fibrous cap is usually poorly developed or absent and marked calcification is rare [4]. All these features make SVG lesions prone to fragmentation and distal embolisation during PCI.

The use of EPD has been a major breakthrough in SVG PCI. A randomised trial enrolling over 800 patients using distal balloon occlusion demonstrated a 42% relative risk reduction of major adverse cardiac events at one month among patients allocated to emboli protection [5]. Most of the benefit was due to a reduction in periprocedural MI (fig. 3). Comparative studies among different type of EPD have followed. Current data suggests that filter devices, distal balloon occlusion devices and proximal occlusion devices may convey similar benefits [6, 7]. Conversely, pharmacologic prevention of distal embolisation by means of glycoprotein IIb/IIIa receptor inhibitors was found of no benefit for SVG PCI. Accordingly, a pooled analysis of five large-scale randomised trials including over 600 patients undergoing bypass graft intervention detected no benefit from active treatment compared with placebo [8]. The likely explanation for this failure is that the amount and/or the composition of the material embolised during the procedure may overwhelm the capacity of these agents to protect the distal vasculature. Data from a large United States registry demonstrated that, despite the strong data supporting its use, EPD are currently deployed in <25% of SVG PCI [9]. In summary, mechanical emboli protection should be applied whenever feasible during PCI of SVG while no GP IIb/IIIa blockade is necessary. Importantly, this does not apply for intervention of arterial grafts (no data).

Figure 2

A Coronary angiogram of a 26-year-old smoker with no angiographic evidence of coronary atherosclerosis but a large coronary thrombus in the proximal and mid portion of left anterior descending coronary artery (LAD), partially obstructing flow.

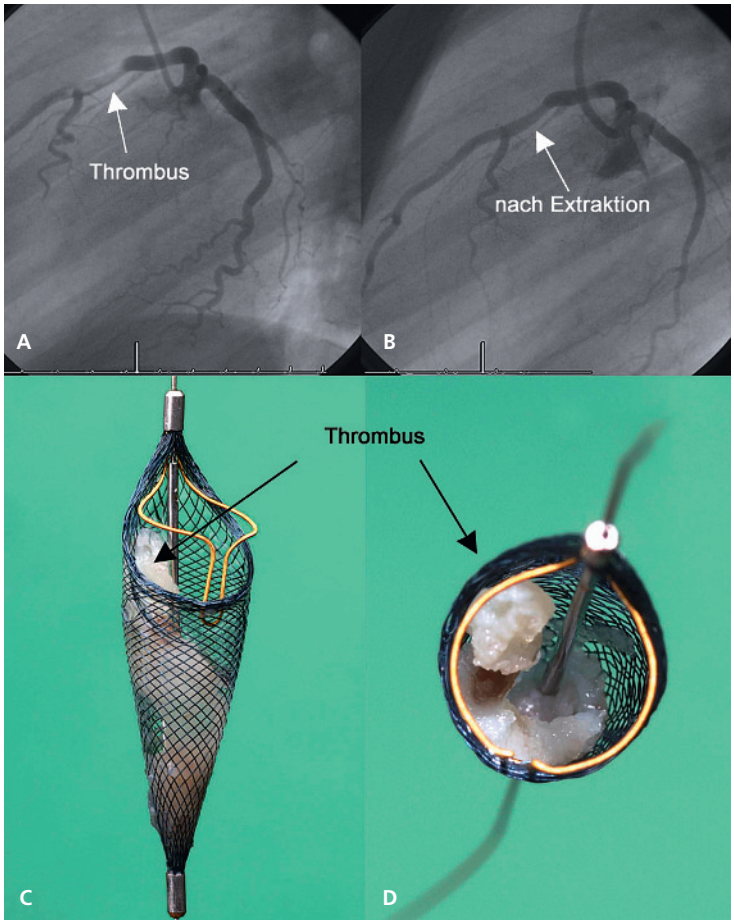
B Despite administration of aspirin, clopidogrel, unfractionated heparin, abciximab, and 20 mg of intracoronary r-tPA the thrombus persisted.

C In an unconventional – off label – way, direct thrombus extraction was performed by introducing a filter protection device into the mid LAD beyond the thrombus.

D The open device was gently pulled back so that the thrombus could be entirely trapped within the filter and then removed using a retrieval sheath. Final angiogram showed complete thrombus removal and no evidence of distal embolisation.

E, F The filter contained a large thrombus.

(Reproduced from [25]: Surder D, Kucher N, Eberli FR, Roffi M. Intracoronary thrombus in a 26-year-old man. Eur Heart J. 2006;27(22):2631. With kind permission, Copyright © 2009, Oxford University Press, Oxford, UK.)



Carotid artery stenting

Distal embolisation remains the most feared complication of carotid artery stenting (CAS), although its incidence can be reduced by proper technique, adequate antithrombotic therapy, and the use of EPD. Virtually any step of the procedure may be associated with debris formation. The two most critical steps in this respect are the engagement of the common carotid artery with the guiding catheter or sheath and the postinfla-

Figure 3

Adverse cardiac events among 801 patients undergoing vein graft interventions randomised to emboli protection (distal balloon occlusion) or no protection. Data extracted from [5].
D = death; MI = myocardial infarction; R = revascularisation.

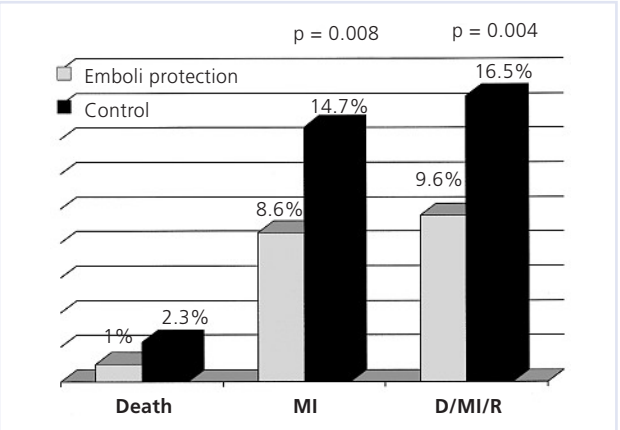
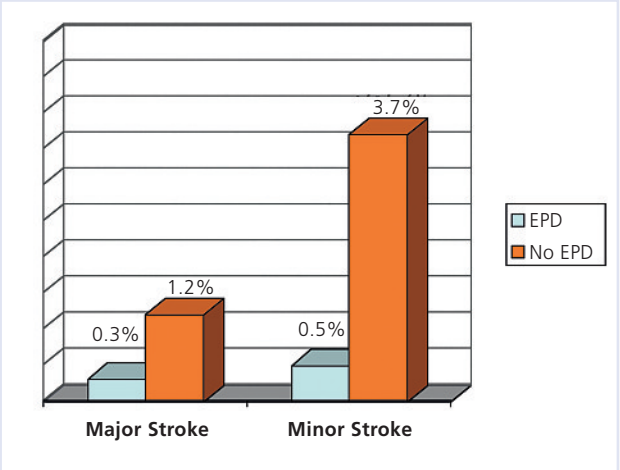


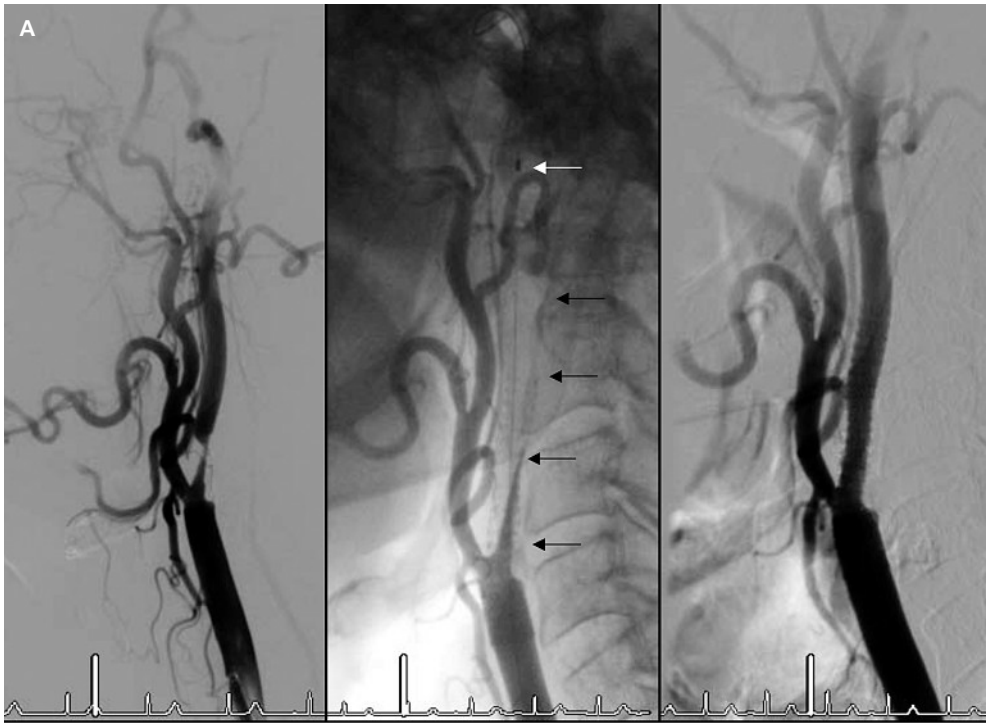
Figure 4
Systematic analysis of the periprocedural ischaemic complications following carotid artery stenting up to the year 2002.
Data extracted from [12].
EPD = emboli protection devices.



tion of the stent [10]. The initial need for EPD came from transcranial Doppler studies demonstrating that, though in most cases clinically silent, embolic signals could be detected in virtually all cases of surgical and endovascular carotid revascularisation. Accordingly, new lesions on diffusion-weighted MRI following non-protected CAS may be documented in over half of the patients [11]. A systematic review including 2357 patients undergoing unprotected CAS and 839 patients stented with adjunctive EPD documented a 30-day death or stroke rate of 5.5% and 1.8% (p <0.001), respectively (fig. 4) [12]. A German prospective CAS registry assessing 1483 procedures detected an in-hospital death or stroke rate of 2.1% among 666 patients undergoing CAS with adjunctive EPD and an event rate of 4.9% among 789 patients treated without EPD. Even after correcting for baseline characteristics the use of EPD was identified as independent protective factor (adjusted OR 0.45; 95% CI: 0.2–0.9; p = 0.026) [13]. Similarly, in a multicenter feasibility trial of CAS performed in 261 patients with and without EPD the one-year major ipsilateral stroke rate was significantly lower among patients undergoing CAS with adjunctive EPD (0% vs 2.3%, p = 0.05) [14].

As a possible confounding factor, EPD have been used more recently and therefore likely at a later stage of the operator's learning curve. Nevertheless, even in large volume centers, the use of EPD positively impacted outcomes. The placement EPD during CAS has been widely embraced, particularly within the community of interventional cardiologists. In our experience, EPD may be utilised in 95% of cases [15]. As correlated of distal embolisation during filter-based CAS, transient flow obstruction in the internal carotid artery may be observed (fig. 5A,B) [16]. The incidence of this

Figure 5
A Carotid artery stenting in a 82-year-old man with 90% symptomatic stenosis of the right internal carotid artery (ICA). The lesion was easily passed with a filter-emboli protection system and the device was deployed in the cervical part of the vessel (left panel). Following balloon post-inflation of the stent, no flow was detectable in the ICA (middle panel). Following aspiration of the carotid blood column the filter was retrieved with good angiographic result locally and intracranially in the absence of symptoms (right panel).
B Inspection of the retrieved filter showed a large amount of debris trapped in the device.



phenomenon may differ according to the type of device used [17]. From a clinical perspective, filter EPD and occlusion-based EPD appear to convey similar efficacy [18]. A broadly shared consensus, though not unanimous, supports the use of EPD during CAS despite the lack of randomised trials based on the efficacy data available and the low device-related complication rate (<1%) [19]. In my opinion, CAS should be routinely performed with EPD. If this is not technically feasible, surgery should be considered.

Renal stenting

In order to prevent decline in renal function following renal revascularisation in patients with renal artery stenosis and renal insufficiency, it is currently being explored whether the use of EPD reduce the incidence of periprocedural atheroembolic renal disease (fig. 6). As opposed to the internal carotid artery or aortocoronary bypass grafts, the renal artery is characterised by a short trunk and early branching. These anatomical features limit the ability to protect the distal vasculature with a device. Although protected renal stenting is feasible, its clinical relevance in terms of preservation of renal function remains to be determined [20]. Encouraging appear the results of a French series showing no deterioration in renal function at six months among 45 patients treated under the protection of distal balloon occlusion [21]. Investigators from New Zealand have reported that among 63 patients with renal artery stenosis and renal dysfunction filter-protected renal stenting was associated with stabilisation or improvement of renal function in 97% of cases at six months, whereas in 3% of the patients renal function further declined [22]. Potentially, the use of this device could have deleterious effects including the need for longer catheter manipulations or the administration of a larger amount of contrast medium. In addition, the effects of microembolisation in the kidney are clearly less devastating than in the brain. Until randomised data assessing the efficacy of EPD become available, embolic mechanical protection cannot be advocated during percutaneous renal interventions.

Conclusions

EPD have a solid stand in the modern armamentarium of the interventionalist. However, the use of these devices is associated with a broad range of benefits in different cardiovascular territories. The most compelling data for mechanical emboli protection are available for percutaneous coronary interventions of aortocoronary vein grafts. In this setting, randomised studies have shown that the use of EPD is associated with a significant reduction in major adverse events. Nevertheless, current registry data suggest that the devices are used only in a minority of those cases. A strong consensus, though not unanimous, supports mechanical emboli protection for carotid artery stenting. In acute MI, the routine use of EPD was not found to be beneficial. Nevertheless, these devices may be considered in selected cases with large thrombus burden. With respect to renal stenting, the experience is still at an early stage and the use of these EPD cannot be recommended.

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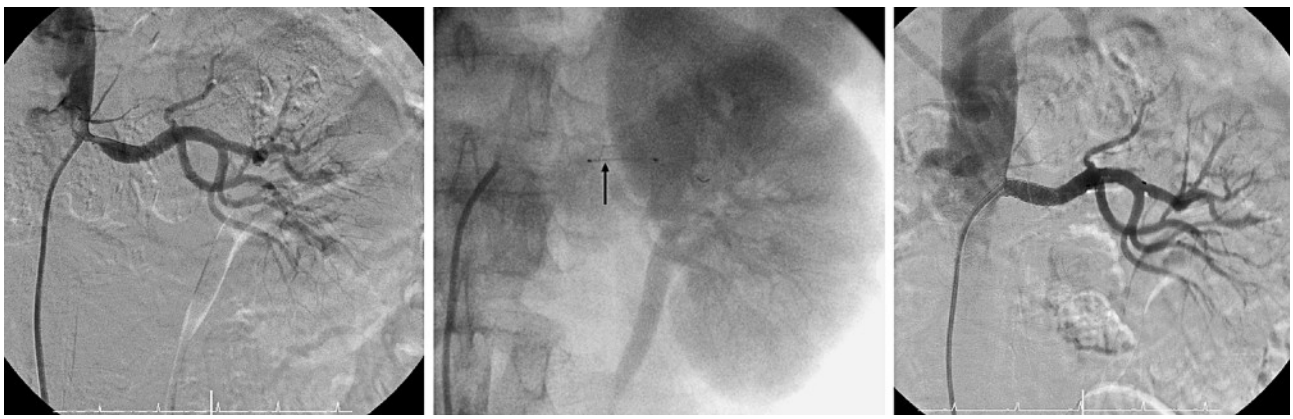
Figure 6
Stenting of the left renal artery using a filter emboli protection device. Digital subtraction angiography demonstrates an ostial stenosis (left panel). In the middle panel, the arrow denotes a filter for emboli protection which is in place throughout the procedure and at the same time has guide wire function. The result following stenting is demonstrated in the right panel. (Reproduced from [20]: Roffi M. Angioplasty for renal artery stenosis: technical improvements and results. In: Electronic Update of the 7th edition of the Textbook Braunwald's Heart Disease. Zipes DP, Libby P, Bonow RO, Braunwald E, editors. Philadelphia: Saunders; 2006. Copyright © 2009, Elsevier, Oxford, UK.)



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