Outflow protection filters during percutaneous recanalization of lower extremities’ arterial occlusions: a pilot study

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Abstract

Purpose: Filter devices are already employed for the protection of carotid, coronary and renal distal vascular bed during endovascular procedures. This is a pilot study investigating their feasibility, safety and distal emboli protection capability during recanalization of lower extremities’ acute and subacute occlusions.

Materials and methods: Study population included 16 patients, 11 with a subacute arterial occlusion and 5 with an acute episode. The Trap filter (Microvena, USA) and its successor the Spider filter (EV3, USA) were utilized. Subacute occlusions were dealt with standard angioplasty and stenting procedures, while acute ones were managed primarily with Angiojet rheolytic thrombectomy. Outflow arterial tree was checked angiographically in-between consequent procedural steps. Embolic material collected after filter recovery was analyzed histopathologically. Patients’ follow-up was scheduled at 1 month.

Results: Seventeen filter baskets were applied in the recanalization of 16 target lesions in total. Mean length of the occluded segments was 6.1 cm (range: 2–15 cm; S.D. = 3.7 cm). Mean in situ time of the filters was 38.75 min (range: 20–60 min; S.D. = 12.71 min). Technical success rate of deployment and utilization of the filtration devices was 100% (17/17). Procedural success rate of the recanalization was 100% (16/16) without any clinical or angiographic evidence of periprocedural distal embolization. Macroscopic particulate debris was extracted from all the filters (17/17) containing fresh thrombus, calcification minerals, cholesterol and fibrin. Mean diameter of the largest particle per specimen was 1702.80 μm (range: 373.20–4680.00 μm; S.D. = 1155.12 μm). No adverse clinical events occurred at 1-month follow-up with 100% limb salvage (16/16).

Conclusion: The application of outflow protection filters is safe, feasible and efficacious in hindering distal embolization complications and safeguarding the distal capillary bed. Nevertheless, this is a pilot study in a limited group. Further studies have to be contacted in order to provide evidence for a more general use of these devices.

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1. Introduction

Periprocedural distal embolization of atherothrombotic particulate debris during percutaneous coronary and carotid interventions is commonly incriminated for obstruction of the microvascular bed, or even larger vessels, resulting in distal infarcts and end-organ dysfunction. Enzymatic analysis and pathologic evidence have demonstrated that subclinical infarction and myonecrosis occur in 5–10% of native coronary vessels and 10–20% of saphenous vein grafts during percutaneous coronary interventions [1]. In the carotid arena, upstream emboli shower during carotid angioplasty and stenting has been well documented by the application of transcranial Doppler [2], leading to an approximate 5% periprocedural major stroke or death rate [3]. The distal renal microcirculation seems to be endangered as well during renal endovascular procedures [4]. Various distal occlusive
and non-occlusive protection devices have emerged in scope of preventing outflow embolization [5]. This is a pilot study evaluating the feasibility, safety and efficacy of an outflow protection filter device (the Trap filter – Microvena, USA – and its successor, the Spider filter – EV3, USA) (Fig. 1) in the recanalization of acute and subacute occlusions of the lower extremities’ arteries.

2. Materials and methods

2.1. Study population

Between September 2002 and December 2003, 16 consecutive patients (mean age = 60 years old; S.D. = 7; 13 males and 3 females) underwent one filter-protected interventional therapy of lower extremities’ arterial occlusions. Patient eligibility was limited to a medical history of acute (1–15 days) or subacute (15 days to 3 months) critical limb ischemia and occlusion of the major vascular supply of the lower extremities, which was indicated by duplex scanning and was furthermore documented by digital subtraction angiography. Technical inclusion criteria to be met were firstly target vessel diameter up to 6 mm, secondly guidewire passage of the occlusion and thirdly an available non-atherosclerotic intimal landing zone for deployment of the filter device at least 3 cm distal to the occlusion. The Hospital’s Ethical and Scientific Committee approved the study. All patients were informed of the investigational nature of the filter-protection devices and gave written informed consent prior to the intervention. Patients’ demographics and characteristics are outlined in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Value</th>
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</thead>
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<tr>
<td>Age (years) ± S.D.</td>
<td>60 ± 7</td>
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<tr>
<td>Males</td>
<td>13</td>
</tr>
<tr>
<td>Females</td>
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</tr>
<tr>
<td>Diabetes</td>
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<tr>
<td>Hyperlipidemia</td>
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<td>Smoking</td>
<td>5</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>0</td>
</tr>
<tr>
<td>Previous intervention of target vessel</td>
<td>3</td>
</tr>
</tbody>
</table>

2.2. Filter devices

The Trap distal protection device (Microvena, USA) features a self-expanding nitinol braided filter basket mounted on a concentric PTFE coated 0.014″ stainless steel wire. The filter basket is heparin coated allowing a maximum 60 min time period of implantation before in situ clotting according to product guidelines, and comes in various diameters ranging from 2.5 to 7 mm. The device is delivered distal to the lesion through a conventional 4F glidecatheter. After completion of the intervention, the filter is retrieved by a heparin-coated funnel through a 5–6 Fr recovery catheter (Fig. 1a). First the funnel is deployed proximal to the filter to prevent dispersion of the collected debris; second the filter is withdrawn within the protective funnel and finally both are collapsed and extracted through the recovery catheter. The Spider distal protection device (EV3, USA) features almost the same technical characteristics, but it is mounted on an eccentric 0.014″ PTFE-coated steel wire, acquires a more conical shape after delivery and is retrieved by direct collapse inside a 4.2–4.9 Fr monorail recovery catheter without the need for the funnel (Fig. 1b). Both devices have gold radiopaque markers on the filter baskets and on the tip of the delivery and recovery catheters, which easily navigate deployment and retrieval under fluoroscopy. The landing zone of the filters is approximately 2 cm distal to the target lesion. Both filters exhibit variable pore size, gradually increasing from the bottom towards the periphery. The estimated average pore size of the mesh of both devices is 100 μm according to product specifications.

2.3. Interventional procedure

All patients were on clopidogrel (75 mg/day) and aspirin (100 mg/day) oral treatment prior to intervention. In case of emergency revascularization without the above premedication, a loading dose of 300 mg clopidogrel and 500 mg aspirin were administered. During the intervention all patients received a non-weighted heparin dosage (5000 IU at the beginning and another 1000 IU/h during the procedure, maximum total dose 10,000 IU).
Using either ipsilateral antegrade or contralateral retrograde puncture of the common femoral artery, a 6F short Terumo or 7F long Arrow (cross-over technique) sheath was placed. The target vessel was selectively catheterized and the occlusion was crossed by means of a 0.035” hydrophilic guidewire (Terumo, JAPAN), over which a 4F glidecatheter (Terumo, JAPAN) was meticulously manipulated 3–4 cm distal to the occlusion. The filter device (both Trap and Spider) was then deployed by slowly retracting the catheter backwards when its distal radiopaque marker had reached the tip of the catheter. In case of acute occlusions, first rheolytic thrombectomy with the Angiojet device was performed. Should rheolytic thrombectomy failed to accomplish removal of the majority of thrombus, adjunctive low-dose intra-arterial thrombolytic therapy was administered.

Second, the underlying atherosclerotic stenosis was treated with angioplasty and stenting if necessary (stenting indications were elastic recoil, intimal dissection and residual stenosis >30%). In the setting of a subacute arterial occlusion, angioplasty and stenting if necessary were performed. Monorail and over the wire 0.018” compatible balloon and stent platforms were utilized. Subsequently, the filter basket was retrieved. In case of Trap the filter was retrieved by its own recovery catheter, which deployed the protective funnel proximal to the filter, allowing the simultaneous withdrawal of both of them. In case of Spider, the basket was extracted either by its own monorail retrieval catheter or by a Terumo 4F glidecatheter; internal diameter available was 0.0038”, if maintenance of the selective vessel access was desirable. In both devices, the final step before extraction was a slow push.
of the recovery catheter forwards until the whole filter mesh was collapsed inside the catheter, as indicated fluoroscopically by the position of the radiopaque markers. It is noteworthy that during the procedure extra care was taken so that the position of the filter was regularly checked and forceful maneuvering of the guidewire was avoided, so as to prevent dislodgement of the protection device leading to vasospasm or potential intimal shearing. Time measurements of the in situ stopover of the filters were taken. In order to regularly inspect the outflow arterial tree and record the exact timing instant in case of complication (distal embolization), digital subtraction angiography was carried out firstly before and after filter delivery, secondly following completion of interventional actions and preceding filter extraction, and thirdly after protection filter recovery (Fig. 2).

After the conclusion of the intervention, antiplatelet therapy was administered to all patients with a combination of clopidogrel (75 mg/day) and aspirin (100 mg/day) for 3 months; aspirin was then prescribed indefinitely. Primary endpoints were firstly technical success, defined as successful deployment and uncomplicated utilization of the filtration devices; secondly procedural success, defined as successful recanalization without any periprocedural distal embolization and residual atherosclerotic stenosis of the target lesion less than 10%; and finally limb salvage indicated by the amputation rate at 1-month follow-up, which was carried out clinically by physical examination and diagnostically by duplex scanning.

### 2.4 Histopathologic analysis

Immediately after extraction, the filter baskets were removed from the guidewires on which they were premounted, flushed with heparinized saline to washout any de novo thrombus and fixed in formalin. The specimens were transferred to the pathology laboratory for further histopathologic analysis. The filters were cut open across their long axis and the captured particulate debris was obtained using microforceps. The specimens were embedded in paraffin and cut into microslides. All hematoxylin and eosin-stained slides were examined and digitally photographed under optical microscopy (200×). Size measurements of the largest particles per slide of each specimen were carried out under a micrometric lens. Particles were classified into macroemboli, if their largest diameter was measured more than 100 μm, or microemboli if it was less than 100 μm. Primary endpoint was the acquirement of macroembolic atherothrombotic debris by the filter devices.

### 3. Results

#### 3.1 Procedural

Percutaneous filter protected lower extremities’ recanalization was performed in 16 patients, involving 16 target lesions in total, corresponding to 16 endangered limbs. The anatomic location and length of the target lesions treated are summarized in Table 2. Fifteen procedures were performed on occluded native arteries, while in one case a femoropopliteal bypass PTFE graft was recanalized. Contralateral retrograde arterial access and cross-over technique was performed in the case of the external iliac artery occlusion and in two cases of superficial femoral artery obstruction, while in the rest of the cases an ipsilateral antegrade arterial access was carried out. The mean length of the occluded segments, measured angiographically, was 6.1 ± 3.7 cm (range: 2–15 cm). In total 17 filters were deployed, including six Trap and 11 Spider devices. In the aforementioned case of the PTFE graft recanalization, two Spider baskets were employed due to massive thrombus debulking. When fluoroscopy depicted blood flow obstruction at the level of the filter with proximal stasis of contrast after the first rheolytic thrombectomy attempt, the first filter was extracted (Fig. 3) and exchanged with a second one for the rest of the intervention.

The diameter of the protection filters was chosen in accordance to the respective vessel’s distal diameter, allowing up to 1 mm oversizing. The mean diameter of the distal arterial landing zone was 4.81, S.D. = 0.83 mm. The size of the filters used ranged from 4 to 6 mm. The mean in situ time of the filters was 38.75 ± 12.71 min (range: 20–60 min).

![Fig. 3. First extracted filter in the case of graft recanalization. Excessive bulk of thrombus is collected which protrudes through the filter mesh.](image-url)
In five cases acute thrombotic occlusions were treated, while in the rest of the subjects 11 subacute occlusions; as-
sessed according to medical history and chronicity of symp-
toms; with a mean estimated age of occlusion 2.0 ± 0.5
months (range: 20 days to 3 months) were recanalized. In
two cases from the acute group and one from the suba-
cute group thrombosis occurred in-stent following recent
endovascular procedures. In three patients with an acute
occlusion, a loading dose of clopidogrel (300 mg) and as-
pirin (500 mg) was administered since the patients were
not receiving any antiplatelet medications. Angioplasty
thrombectomy with the Xpedior catheter (one catheter per
limb, catheter size 6F, duration of activation 5–9 min) aided
by adjunctive low-dose local thrombolysis (200,000–350,000
units urokinase), in case of mural thrombi remnants, suc-
cceeded in restoring blood flow in that group. In two cases
balloon dilation of an underlying stenosis was required,
while in another two cases stenting was performed due
to unsatisfactory ballooning outcome. All subacute occlu-
sions were dealt with conventional angioplasty and stent-
ing techniques without lysis administration. Balloons and
stents were chosen according to availability without any
particular preference criteria. In total 10 of the 11 lesions
were stented. In one case vasospasm occurred, which grad-
ually resolved after local intra-arterial 0.3 mg nitroglycerine
infusion. No intimal laceration was observed angiographi-
cally in the filter landing zones. Technical and procedural
success rate as predefined reached both 100% (17/17 and
16/16, respectively), without any angiographic or clinical
signs of distal embolization. At 1 month no adverse clinical
events occurred and primary patency demonstrated by du-
plex scanning was 100% (16/16). No surgical debridement
or amputation was necessitated and limb salvage rate was
100% (16/16).

3.2. Histopathologic

In total 17 filters were examined. All filters had macro-
scopically visible collections of particulate debris after re-
treval. Hematoxylin–eosin stain of the microslides and
observation under optical microscopy revealed erythro-
cytes, fibrin conglomerates and calcifications in all speci-
mens. Cholesterol crystals were traced in 5 subacute cases.
Larger amounts of fresh thrombus were observed in all
extracts recovered from acute occlusions. In one speci-
men that was extracted from a subacutely occluded na-
tive artery, acute inflammatory cells were detected as well.
In the case of the occluded femoropopliteal PTFE by-
pass graft hemodeserin traces were encountered. Macrom-
boic and accompanying microembolic debris were de-
tected in all specimens (17/17). Mean diameter of the
largest particle per slide was 1702.80 (a wide variety of
particle sizes have been observed ranging from 373.20
to 4680.00 μm, S.D. = 1155.12 μm). Debris was also af-
fixed to the filter mesh and could not be completely
harvested.

4. Discussion

In the editorial of David O. Williams it is stated that dur-
ing the first in man coronary balloon angioplasty, Andreas
Gunther and Vorwerk [12] first described the novel tech-
nical concept of utilizing a miniaturized Dormia embolec-
tomy basket as a distal protection device more than a decade
ago. This is a pilot study that focused in the evaluation of
a non-occlusive distal protection filter basket in lower ex-
tremities’ recanalization procedures, which usually deal with
multilevel disease and heavy atherosclerotic burden. Unlike
distal balloon occlusion (such as by Percusurge Guidewire
device) which completely blocks blood flow, raises the risk
of thrombosis due to stasis and limits the available time pe-
riod to intervene, distal filter protection does not interrupt
blood flow and achieves a longer period of outflow protec-
tion (up to 60 min in our study) throughout the primary and
any secondary revascularization procedures. The filter de-
vices under investigation (Trap and Spider) proved to be safe
and their application in the lower extremities’ major arterial
tree was feasible reaching 100% technical success rate, both
in the delivery and retrieval process. No troubleshooting oc-
curred during the unprotected crossing of the lesion and distal
advancement of the 4F glidecatheter in order to deploy the
protection filter. Flow obstruction was imaged fluoroscopi-
cally in one case due to heavy thrombotic burden captured
by the basket and was managed by exchanging the filter with
a second one. Should fluoroscopy depict that atherothrombotic
debris almost fill or even exceed the filter basket’s capacity, care must be taken to avoid squeeze or spill of the embolic material. Hence it would be wise to utilize a retrieval system of larger internal diameter, like a long 6-7F sheath. In even more complex situations a 0.035" safety guidewire may be placed first to augment support during maneuvering and secure vessel access for subsequent interventions in case both filter and sheath are extracted in block. The main technical advantages of the filter devices under investigation are the selection of the operator’s choice of wire to cross the lesion first, the use of a conventional atraumatic 4F tapered glidewire as the delivery vehicle and the ability to preserve selective vessel access after completion of the primary intervention and filter retrieval. Nevertheless, it should be highlighted that the first crucial step of unprotected crossing of the occlusion could potentially generate particles escaping to the periphery. Thus, aggressive interventional maneuvers, which increase embolic hazards, should be avoided. However in our series, angiography that was performed prior and post filter implantation portrayed no distal embolization attributable to the guidewire passage and filter landing action. From the operator’s point of view, in spite of the very cautious manipulations of the interventional instruments, all filters tended to slightly dislodge during the procedure, without however any intimal laceration. The vasospasm that occurred once could be attributed to intimal stress by such a forceful filter movement. Despite the relatively large average pore size (100 μm) of the filter mesh, atherothrombotic particulate debris of variable size was collected in all cases. The debris was always macroscopically visible and measured 1.70 ± 1.16 mm across its largest diameter. In all cases, histopathologic inspection documented a variety of cellular and acellular components, especially fibrin conglomerates and calcifications. A predisposition of fresh thrombogenic particles in favor of the acute occlusions was also observed. However, no statistical comparative analysis according to estimated thrombus age was carried out, because of the small number of cases. The aforementioned findings document that percutaneous thrombectomy, angioplasty and stenting of acute and subacute occlusions produce a shower of macroemboli (>100 μm) endangering distal circulation.

Another recent pilot study by Konig et al. [13] investigated the deliverability and protection capabilities of the Angioguard emboli capture system (Cordis, USA) in peripheral angioplasty procedures. The Angioguard protection device basically consists of a permeable polyurethane membrane with standard 100 μm pore size fixed on nitinol struts. By analyzing the extracted baskets with scanning electron microscopy, the authors detected considerable amounts of microembolic and macroembolic fibrin aggregates. The above are in agreement with our histopathologic report, confirming the high frequency of downstream debris embolization during lower extremities’ endovascular operations. We traced cholesterol crystals in five subacute cases, as opposed to Konig et al. [13] who detected minimal lipid traces after angioplasty of chronic stenotic lesions. This discrepancy is probably owed to anatomic and pathophysiologic differences between chronic stenoses and arterial occlusions.

Nevertheless, the Angioguard protection study suffered from increased downstream embolization incidence (67%), which was not encountered in our study. The authors treated those cases with percutaneous thrombectomy or thrombolysis and vasodilators. The aforementioned high frequency of distal embolism complications was attributed to platelets’ aggregates and monomeric fibrin deposition on the Angioguard membrane, which were conglomerated and presumably extruded from the basket during filter closure, thus eluding to the periphery [13]. However, in our study no case of distal periprocedural embolism befell, despite the detection of debris affixed to the filter mesh and similar filter withdrawal maneuvers. The above discrepancy in debris embolization capacity could be pertinent to the different technical characteristics of the Trap/Spider filter and the Angioguard basket: better conformability of the first against the luminal wall, variable versus standard pore size, more conical shape of the Spider filter; or even to different features with regard to in situ chemical interaction with platelets, fibrin formation, and squeeze mechanics during the crucial final step of filter extraction. However, signs of corresponding clinical ischemia were reported neither by Konig et al. [13] nor by us. In addition, fibrinous embolic material affixed to the protection device was a common finding in both studies, documenting the potential of both devices to induce thrombosis and formation of fibrin conglomerates in situ [13]. It is also worth mentioning that apart from the potential mechanical obstruction and perfusion defects, embolic debris is also reported to invoke vasospasm and endothelial dysfunction, impeding local rheologic conditions and enhancing thrombogenicity [14]. The application of myocardial contrast echocardiography has documented that more than 25% of patients with successful revascularization procedures and angiographically restored epicardial flow suffer from inadequate tissue reperfusion owing to microvascular obstruction [15]. Thus, outflow protection filters evolve to an important interventional tool in order to safeguard vascular outflow and improve clinical outcome. In our study, long-term follow-up with regard to limb salvage is awaited in order to conclude whether distal filter protection proves clinically beneficial in the protection of the peripheral capillary bed from microemboli, especially in high-risk diabetic limbs.

In conclusion, the pilot application of outflow protection filter devices was safe, feasible and efficacious in hindering macroembolism complications and safeguarding the distal capillary bed during revascularization procedures of lower extremities’ arterial occlusions. Nonetheless, large-scale double-blinded trials are necessary in order to yield statistically significant therapeutic worthiness, determine the optimal technical characteristics and assess the cost-effectiveness of the latest distal protection devices, which have already set higher safety standards in coronary and carotid endovascular procedures.
References


