WIRION™ embolic protection system for carotid artery stenting and lower extremity endovascular intervention

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Aim: To summarize all available literature regarding the Wirion™ embolic protection system (EPS) and present examples from our center. **Materials & methods:** A review of literature was performed about the utilization of Wirion EPS. **Results:** One study was identified investigating the outcomes of Wirion during carotid artery stenting. The study demonstrated 98.3% procedural success with stroke occurring in only 2.5%. Two single arm studies were identified investigating the efficacy of the Wirion filter during lower extremity endovascular interventions. The reported device success ranged from 95.1 to 97.3%. **Conclusion:** While carotid artery stenting should always be performed with adjunctive EPS in order to decrease the risk of cerebrovascular accidents, the routine use of EPS in femoropopliteal interventions remains an active area of investigation.

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Peripheral artery disease (PAD), including femoropopliteal and carotid artery disease, affects more than 8 million patients in the USA [1,2], with its prevalence increasing by almost 24% from 2000 to 2010 [2,3]. The American College of Cardiology/American Heart Association guidelines have recommended that revascularization is a reasonable treatment option for patients with symptoms of lifestyle limiting claudication, when appropriate medical therapy ± exercise fail to control symptoms [4]. Endovascular revascularization has been increasingly utilized for PAD, especially for those at high risk for open surgery, and is indicated for almost all patients with rest pain or a nonhealing wound due to critical limb ischemia [5–8].

Distal embolization (DE) occurs commonly after percutaneous transluminal angioplasty (PTA), being clinically apparent in 2–5% of the patients who undergo endovascular interventions [9–14]. A retrospective analysis by Shammam *et al.* investigating the incidence of DE in 577 patients undergoing PTA for PAD, demonstrated that 2.4% of the cases eventually required further mechanical or pharmacologic therapy for periprocedural DE [14]. DE after PTA is a major concern as it has been associated with severe ischemic adverse events (i.e., outflow compromise and eventually amputation after infrainguinal PTA, devastating ischemic stroke after PTA for carotid lesions) [14,15]. As such DE is also correlated with longer overall procedural time, fluoroscopy time, contrast utilization, overall radiation exposure and in-hospital stay [14,15].

Several lesion (e.g., thrombotic, calcified lesions, ulcerated atherosclerotic plaques, chronic total occlusions, TASC C–D lesions etc.) [8–11,16] and device related characteristics (e.g., rotational/directional atherectomy utilization, cutting/scoring balloon catheters etc.) [16–21] have been correlated to higher periprocedural DE rates, with several reports suggesting an incidence of DE up to 100% after endovascular infrainguinal interventions utilizing rotational atherectomy [16–21]. Therefore, distal embolic protection devices (EPD) have been developed to prevent distal macro and microdebris embolization providing assurance and protection from procedural complications [22–27]. EPD can be utilized in several endovascular interventions, including PTA for carotid and femoropopliteal disease.

Carotid artery stenting (CAS) can be used for the treatment of severe carotid disease [28]. However CAS is limited due to higher risk for periprocedural ischemic stroke, which is mainly attributed to DE of atherosclerotic

plaque material [29,30]. Additionally, DE has been correlated with cognitive dysfunction [31] and postprocedural memory decline [32]. Thus, CAS should always be performed with adjunctive EPD in order to prevent the sequelae of DE. Therefore, several distal or proximal embolic protection systems (EPS) have been developed for adequate neuroprotection during CAS [33–35]. However, in contrast to carotid interventions where the EPD utilization is mandatory, the routine use of EPS at the femoropopliteal segment remains an active area of investigation, as DE at this segment is rarely clinically significant. Thus, the aim of this manuscript was to present our experience using Wirion™ EPS (Cardiovascular Systems, Inc, MN, USA) and to summarize all available literature regarding its performance at the infrainguinal and carotid segments.

Materials & methods

Device description (design & deployment)

The Wirion EPS consists of a distal filter (filter basket and locking mechanism) and a rapid exchange delivery catheter. The exchange catheter has a 1.1 mm crossing profile and can be mounted on any 0.014-inch guidewire and via 6F or greater guiding catheters. The filter basket is made of a self-expanding nitinol scaffold and a nylon filter membrane with 100-µm pores (~1000/filter). The filter can efficiently be deployed in vessels with a diameter ranging from 3.5 to 6.0 mm and at any location along the guidewire, using a proprietary remote locking system (handle at the proximal end of the delivery catheter). After completion of the endovascular intervention (e.g., atherectomy, stenting and balloon angioplasty), the filter can be retrieved utilizing a retrieval catheter with a retractable tip. The retractable tip of the catheter facilitates smoother passage through the stented area when stents are deployed, thereby minimizing the risk of entanglement.

Case series design (endovascular treatment; definitions & outcomes)

This case series included 13 consecutive patients undergoing endovascular interventions for lifestyle limiting claudication (Rutherford classification 3), attributed to femoropopliteal disease. In all cases, atherectomy was performed additional to PTA and the Wirion filter was used for embolic protection. The study was approved by the Institutional Review Board and all HIPPA rules were adhered to. Heparin was administered in all cases and after the lesion was crossed the filter was deployed distally. The filter was retrieved after completion of atherectomy or scoring balloon utilization.

Study selection & data extraction

Systematic searches were conducted in PubMed/Medline, Scopus and Cochrane Central according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [36]. These databases were reviewed for prospective or retrospective analyses reporting on outcomes and/or complications of endovascular interventions with utilization of the Wirion EPS and the search terms used were: ‘Wirion EPS’, ‘Wirion embolic protection system’, ‘Wirion’. The search was conducted independently by two investigators, blind to each other and disagreements were resolved by consensus. The references of the included studies were also manually reviewed to identify further eligible articles.

Studies included in this systematic review fulfilled the following criteria: studies reporting on short- and long-term outcomes of any type of endovascular intervention for PAD utilizing the Wirion EPS; studies published until February 2020. The PRISMA flow diagram is illustrated in [Figure 1](#). Two reviewers independently extracted the relevant data from the eligible studies. All disagreements were resolved following discussion and the final decision was reached by consensus. Data were extracted for patients’ baseline characteristics and angiographic procedural outcomes. However, due to between-study differences in lesion characteristics and the reporting methods, the findings were summarized from each study, but the results were not pooled. As no comparative analyses were performed, the risk of bias was not assessed, however results are provided separately for each of the included studies.

Results

Wirion filter utilization during CAS

One study was identified across literature reporting on performance of the Wirion EPS in patients undergoing CAS (NCT01783639) [37]. This was a prospective, multicenter, single-arm study enrolling 120 high surgical risk patients that underwent CAS for ≥ 50 and $\geq 80\%$ stenosis in symptomatic and asymptomatic carotid disease, respectively [37]. The study demonstrated 98.3% procedural success and 100% periprocedural survival rate, with stroke occurring in only 2.5% of the cases [37]. The authors also compared the performance of the Wirion EPS to

Figure 1. PRISMA search flow diagram. February 2020.

a historical control groups of CAS with utilization of independent distal filter EPD [22,23,25,26] and demonstrated lower periprocedural death, stroke and myocardial infarction in the Wirion group (3.3%) versus the historical control group (6.3%; $p < 0.001$) [37]. Thereby the authors suggested that advancements in EPDs may be related to the observed improvement of neuro-protection with the Wirion EPS [37].

Figure 2. A 62 year old man presented with internal carotid artery stenosis greater than 70%. (A) The patient was deemed to be too high risk for carotid endarterectomy and as such a percutaneous strategy was pursued. A Wirion™ EPS was used for embolic protection (red arrows) (B-E). The vessel was pre-dilated and then a 8-10x40mm Xact stent was deployed (B). The stent was post-dilated for better stent expansion (C). No significant residual stenosis was detected by angiogram (D). The filter was retrieved successfully (E,F) without any angiographic complications occurred (G). The post-operative course of the patient was clinically uneventful.

In our center, three patients with severe carotid disease, deemed as high risk for surgery, underwent CAS with the utilization of the Wirion EPS. Patient and procedural characteristics of the patients are presented in [Supplementary Table 1](#). In all three cases, the Wirion filter was successfully deployed and retrieved after completion of the endovascular procedure. Three cases were treated with tapered bare metal stents, while in one case adjunctive intravascular lithotripsy was performed before stenting due to the presence of severe calcific disease. No DE occurred peri-procedurally, and the patients had an uneventful postoperative course (i.e., no cerebrovascular adverse events). An example of Wirion use at the carotid segment is illustrated in [Figure 2](#).

Wirion filter utilization during femoropopliteal angioplasty

Two single arm studies and one case report were identified investigating the efficacy of the Wirion filter during lower extremity endovascular interventions. Patient and procedure characteristics are summarized in [Table 1](#), while data on device success and periprocedural outcomes are presented in [Table 2](#). Shammas reported the first case of Wirion EPS for the treatment of femoropopliteal disease [38]. The authors presented a case of a 62-year-old male with atherosclerotic risk factors and lifestyle limiting claudication attributed to occlusion of the mid/distal superficial femoral artery (SFA) [38]. SFA endovascular revascularization was performed uneventfully (successful filter deployment/retrieval), with no DE occurring [38].

The WISE LE (WIRION EPS in Lower Extremities Arteries; NCT02780349) study was a multicenter study investigating the safety and efficacy of the Wirion EPS during 103 endovascular procedures for lower extremity symptomatic PAD [39]. Shammas *et al.* reported 95.1% (n = 98/103) device success, defined as successful

Table 1. Patient and procedure characteristics.

Study	Total	Age (years)	M	Caucasian	CAD	Smoking history	DM	HLD	HTN	CHF	RC	Lesion location	Previous lower extremity procedures	De novo lesions	Atherectomy type	Balloon angioplasty	Stenting	Ref.
Shammas <i>et al.</i> (2018)	103	68.2	68.9%	95.1%		79.7%	46.6%	92.2%	93.2%	14.6%	2–4%	SFA	72.8%	65%	32 directional, 9 laser, 21 orbital, rotational 51	72 DCB, 25 BA	26	[39]
Sharis <i>et al.</i> (2018)	37	68.7	64.9%		64.9%	81.1%	51.4%	100%	89.2%	0.0%	3–5%	SFA		40.5%	rotational 37	26 DCB, 11 BA	4 DES, 5 BMS	[40]
Shammas <i>et al.</i> (2016) (case report)	1	62.0	M		no	yes	yes	yes	yes	no	3%	SFA			1 rotational	1 DCB	1 BMS	[38]
Our cohort	13	67.2	12%	91.7%	38.5%	84.6%	38.5%	92.3%	92.3%	0.0%	3%	SFA	53.8%	100%	4 rotational, 3 orbital, 4 laser, 2 directional; +9 angiosculpt	12 DCB, 1 BA	2 DES, 3 BMS, 1 covered stent	
CAD: Coronary artery disease; CHF: Congestive heart failure; DM: Diabetes mellitus; HLD: Hyperlipidemia; HTN: Hypertension; N: Number of patient; M: Male; RC: Rutherford classification; SFA: Superficial femoral artery.																		

Table 2. Periprocedural outcomes.

Study	Patients total	Death	Acute MI	Thrombosis	Pseudo-aneurysm formation	Dissection at filter site	Perforation	Distal embolization	TVR	Device success	Ref.
Shammas <i>et al.</i> (2018)	103	0	0	0	1	0	0	0	1	98	[39]
Sharis <i>et al.</i> (2018)	37	0		0		0		3 (only severe)		36	[40]
Shammas <i>et al.</i> (2016) (case report)	1	no	no	no	no	no	no	no	no	1	[38]
Our cohort	13	0	0	0	0	0	0	0	0	13	

N: Number; MI: Myocardial infarction; TVR: Target vessel revascularization.

delivery/deployment of the Wirion filter distally to the lesion and filter retrieval without any complications [39]. In three cases, another Wirion filter was successfully deployed, while in two cases the failure of device deployment was attributed to a kink in the guidewire that required its exchange [39]. Based on the very low frequency of periprocedural complications, the authors suggested that the Wirion is not inferior to other commercially available independent filters used for distal embolic protection (e.g., SpiderFX) [39].

Sharis *et al.* studied 37 patients undergoing femoropopliteal angioplasty with adjunctive rotational atherectomy (i.e., Jetstream atherectomy) [40]. All patients presented with a Rutherford category ranging from 3 to 5 and lesions being TASC A/B in 75.7% of the cases (mean lesion length: 150.4 mm) [40]. The Wirion filter was used for distal embolic protection in all cases and the reported device success was 97.3% ($n = 36/37$). The one device failure that occurred was attributed to entrapment of the guidewire on the rotational atherectomy device [40].

In our cohort of 13 subjects, in all cases (100%) the Wirion filter was successfully deployed and retrieved without any dissections occurred at the filter site. Additionally, no DE occurred, however in two cases the Wirion filter was full, impeding flow distally. Shammas *et al.* reported no events of periprocedural DE, while a filter analysis showed that the majority (98%) of the particles captured on the filter membrane was <1 mm [39]. Sharis *et al.* reported DE in three cases despite the use of the Wirion EPS, however only one case out of the three was clinically severe and required treatment more than aspiration [40]. The authors also noted that in 51.4% of the overall cases debris was captured by the Wirion filter (14 macro and 5 microdebris cases) [40]. No severe angiographic complications, deaths or acute myocardial infarctions occurred in all three cohorts.

Discussion

This systematic review of literature summarized all available published data regarding the safety and efficacy of the Wirion EPS. Based on the available data, the Wirion distal filter was associated with high technical and clinical success in both the carotid and femoropopliteal vascular beds. These data eventually led to US FDA approval for application of the Wirion EPS at the carotid and the femoropopliteal segments [37,39].

Carotid artery stenosis is responsible for approximately 20–25% of strokes [41]. However, the risk of stroke has been correlated to the symptomatic status of the patient. Thus, patients with cerebrovascular symptoms have an annual risk for ischemic stroke ranging from 10 to 15%, while asymptomatic patients have an annual stroke risk of 2–2.5% [42,43]. Therefore, carotid revascularization, with either CAS or carotid endarterectomy (CEA), has been proposed as a feasible treatment option for carotid stenosis. Indications for carotid revascularization are presented in [Supplementary Table 2](#). CAS has been an accepted alternative option to CEA for patients deemed as high risk for open repair [44,45]. However, the main concern about CAS is the higher risk for DE and the associated risk for periprocedural stroke [46]. Thus, CAS should always be performed with adjunctive EPD or proximal embolic protection in order to decrease the risk of cerebrovascular accidents [27,47,48].

Rosenfield *et al.* compared the outcomes of CAS + EPD to CEA in 1453 patients with asymptomatic carotid artery disease [49]. The authors reported 3.8 and 3.4% combined stroke, death or MI rates in the CAS and CEA groups, respectively [49]. Additionally, the 30-day stroke/death rate was 2.9% in the CAS group versus 1.7% in the CEA group, without any statistical difference between the two approaches ($p = 0.33$) [49]. Therefore, Rosenfield *et al.* concluded that with adequate neuroprotection CAS was not inferior to CEA for the treatment of asymptomatic carotid disease [49]. Furthermore, a prospective multicenter study of 322 patients with carotid stenosis being at high risk for CEA, investigated the safety and efficacy of independent distal filters used for embolic protection

during CAS [50]. The study reported a periprocedural death/stroke/MI rate of 2.3% in the cohort in which a newer filter was utilized [50]. As the periprocedural outcomes of this study were superior to previous, older trials (e.g., ARCHeR trial: 8.3%; SAPPHiRE trial: 6.5%; CABERNET trial: 3.8%) [22,51,52], the authors concluded that the outcomes of CAS have improved over time, which could be attributed to the combination of better EPDs as well as improvement in CAS techniques [50].

Several EPDs for neuroprotection have been developed, including distal or proximal balloons, flow reversal, distal filters and combined techniques. However, device-specific learning curves have limited adoption for many of the commercially available EPSs [53–55]. Operator experience and ability to identify lesion morphological characteristics that are associated with high risk for emboli formation (e.g., ulcerated/soft plaques, long lesions etc.) and proper filter apposition, play an important role in stroke prevention as well [55]. The Wirion EPS, with its unique design, including compatibility with all guidewire sizes, shorter learning curve and safe crossing of the target lesion, is a promising option for distal embolic protection. Furthermore, its easy deliverability allows its deployment even in tortuous vessels [37].

In the WISE trial, 120 patients with severe carotid artery disease underwent endovascular revascularization and the Wirion™ filter was used for DE protection [37]. The operators used up to ten different guidewire types and achieved not only the predefined success criteria but also the 30-day major adverse cardiac and cerebrovascular events were lower compared with historical control studies [22,23,25,26,37]. The authors concluded that the observed clinical benefit could be attributed to the easy use of the Wirion filter (i.e., guidewire-centered delivery system and independent distal filter) and to its unique properties (e.g., retractable nose cone, compatibility with any guidewire etc.) [37]. Therefore, the newer guidewire-centered EPSs (e.g., Wirion), with more ergonomic features, promise better clinical outcomes after CAS.

In addition to carotid cases, during several lower extremity endovascular procedures the utilization of EPDs is necessary as well. Although many studies have reported the presence of embolic debris in filters used during peripheral endovascular interventions, less data are available on the clinical impact of DE in those procedures [56–58]. Lam *et al.* investigated the rate and timing of DE in 60 patients with SFA lesions, undergoing PTA ± stenting with/without adjunctive atherectomy [13]. The authors suggested that debris was detected by a doppler probe, placed distally in the popliteal artery, during every step of the PTA (i.e., crossing, balloon angioplasty, stenting and atherectomy) [13]. However, as only one patient experienced an angiographically and clinically significant DE, the authors suggested that EPDs at the femoropopliteal segment should not be used routinely [13]. Similarly, Shammas *et al.* have reported that macrodebris embolization is common (55%) after directional atherectomy performed for lower extremity arterial lesions, however they have underlined that its clinical significance should be further determined [58].

Routine EPD utilization during endovascular procedures for lower limb PAD cannot be advocated, as limb loss from DE during PTA for lower extremity lesions is rare [13]. However, when it does occur additional therapeutic measures are needed (e.g., aspiration thrombectomy, mechanical thrombectomy etc.) [59], which may increase the overall cost of care and may also damage the distal vessels, leading eventually to long-term adverse events [16,60]. Therefore, distal embolic protection is crucial in cases of advanced PAD with poor distal run off in order to prevent acute limb ischemia and/or amputation.

There have been several lesion and procedural characteristics that have been correlated with high risk for DE [59]. Makino *et al.* in an intravascular ultrasound analysis (IVUS) analysis, found that plaque area was strongly correlated with DE [61]. Additionally, previous reports have suggested that calcified lesions are associated with a higher rate of embolic debris formation [58,60,62,63]. Other lesion characteristics that have been correlated with higher DE risk include but are not limited to chronic total occlusion, in-stent restenosis, thrombotic lesions, long lesions etc [17]. Thus, in the light of this, individualized treatment with proper identification of high-risk lesions and high-risk therapeutic modalities is important in order to prevent from ischemic adverse events that could be avoided with the use of an EPD.

Shrikhande *et al.* provided evidence that the use of directional or orbital atherectomy were associated with the generation of debris that embolized distally, immediately after atherectomy was performed [16]. Furthermore, previous studies reported that DE occurred in up to 10% of patients treated with rotational atherectomy for infrainguinal disease [64,65], while in some cases the DE rate reached almost 100% [16–21]. Interestingly, the ‘Preventing Lower Extremity Distal Embolization Using Embolic Filter Protection’ (PROTECT) study, investigating the incidence of significant embolization material after PTA for lower extremity PAD, demonstrated debris in 55% of the cases [58]. The heterogeneity in the reported results could be attributed to different devices utilized and to

the different lesions treated. However, it could be concluded that when atherectomy devices or cutting/scoring balloons are utilized the risk for emboli generation is high, regardless the type of lesion and as such EPD use is reasonable.

Challenging PAD lesions (e.g., long femoropopliteal TASC D lesions, heavily calcified infrapopliteal lesions, poor distal run-off etc.) can now be successfully treated with endovascular techniques, however the use of more invasive modalities, such as atherectomy, intravascular lithotripsy, scoring etc., are often required for more optimal angioplasty result. Therefore, as more and more complex lesions can be treated endovascularly, the EPD utilization has become necessary in the clinical practice. The WISE LE study investigated the safety and efficacy of the Wirion EPS during 103 endovascular procedures for lower extremity symptomatic PAD and demonstrated 95.1% device success, with no severe embolization occurred (i.e., DE requiring therapeutic measures more than aspiration) [39]. Thus, the Wirion was proven to be effective for capturing macro and microdebris, while improving clinical outcomes of lower extremity PTA adjunctive with atherectomy [39]. The efficiency of the Wirion filter has been attributed to its ability of being deployed in vessels with a diameter ranging from 3.5 to 6.0 mm and its compatibility with any guidewire. Thus, these features of the Wirion make it a universal filter for any type of femoropopliteal lesions. However, further research should determine for which type of lesions and which types of procedures the use of an EPD would be cost-effective and clinically beneficial in an effort to optimize medical care of patients with PAD.

Limitations

The results of the present systematic review should be interpreted in the context of several limitations. First, the nonrandomized, observational nature of the included studies limits the generalizability of our results due to potential selection bias. Second, due to between-study differences in lesion characteristics (e.g., treatment of different types of lesions etc.) and the limited number of the overall included studies, results could not be pooled. Additionally, although our experience with the Wirion provided promising evidence, the main conclusions that the Wirion EPS is safe and can be successfully used during either carotid or femoropopliteal PTA is based mainly on the previous published studies by Shammass *et al.* (femoropopliteal cohort) and Scheinert *et al.* (carotid cohort). Last, postmarket surveillance with prospective registries is needed, in order to confirm these promising results about Wirion EPS efficacy and safety.

Conclusion

Further understanding of the role of lesion and procedural characteristics in the formation of atheromatous debris, along with the development of new technologies, will help optimize the outcomes of endovascular interventions and ultimately improve limb salvage. Based on the available data, the use of universal independent distal filters during peripheral endovascular interventions (e.g., Wirion EPS) could shorten the operator's learning curve and provide adequate embolic protection. However, future studies are needed to determine the association of DE and clinically significant adverse events, in order to develop cost-effective treatment algorithms for high risk patients.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/fca-2020-0023

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Summary points

- As more and more complex lesions can be treated endovascularly, the embolic protection device utilization has become necessary in the clinical practice.
- The Wirion™ embolic protection system (EPS) consists of a distal filter and a rapid exchange delivery catheter.
- The exchange catheter can be mounted on any 0.014-inch guidewire and via 6F or greater guiding catheters.
- One study investigated the efficacy of Wirion™ EPS during carotid artery stenting and demonstrated 98.3% procedural success with stroke occurring in only 2.5% of the cases.
- Two single arm studies were identified investigating the efficacy of the Wirion filter during lower extremity endovascular interventions.
- The reported device success at the femoropopliteal segment ranged from 95.1 to 97.3%.
- The Wirion EPS is not inferior to other commercially available independent filters used for distal embolic protection at the carotid or femoropopliteal segment.
- The Wirion EPS's unique properties could shorten the operator's learning curve, while allowing a wide range of application.
- While carotid artery stenting should always be performed with adjunctive EPS in order to decrease the risk of cerebrovascular accidents, the routine use of EPS in femoropopliteal interventions remains an active area of investigation.
- Future studies are needed to determine the association of distal embolization and clinically significant adverse events.
- Cost-effective treatment algorithms for high DE risk procedures/lesions should be developed.

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