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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Technical success and associated economic implications of conventional re-entry devices in subintimal recanalization of femoro-popliteal chronic total occlusions

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PURPOSE

Re-entry devices contribute to the high success rate of subintimal recanalization of chronic total occlusions (CTO). However, to date, there are no studies comparing the available conventional re-entry devices concerning the impact of their technical success on economic aspects, as these devices differ greatly in their acquisition costs. This prospective observational study intends to contribute to this question.

METHODS

Prior to the start of the prospective study, all previous applications of the Outback® in femoro-popliteal CTO since its introduction to our hospital were analyzed retrospectively (n = 31). From June 2018 until January 2020, all patients with femoro-popliteal CTO treated with clear subintimal recanalization were included (n = 109). In the case of failed spontaneous re-entry, either the OffRoad® (study arm I, n = 20) or the Enteer® catheter (study arm II, n = 20) was used. If assisted re-entry failed, the Outback® device was used as a bailout. Baseline demographic and clinical data, morphologic characteristics, and technical success were documented. Additional per-patient costs due to the use of re-entry devices were analyzed.

RESULTS

A retrospective evaluation of all Outback® applications revealed a technical success rate of 97% (30/31). In the prospective study, 63% (68/109) were successfully treated without using re-entry devices. The overall procedural success was 95% (103/109). In study arm I, the OffRoad® achieved a success rate of 45% (9/20), with a subsequent successful application of the Outback® in 80% (8/10) of the failed cases. In study arm II, the Enteer® was successfully employed in 60% (12/20) of cases, and the Outback® was then used successfully in a further 62% (5/8) of cases. Too large a distance between the device and the target lumen was a knockout criterion for all tested devices, leading to a subgroup analysis with the exclusion of three cases, resulting in a success rate of 47% for the OffRoad® and 67% for the Enteer® device. Furthermore, in severe calcification, only the Outback® reliably enabled revascularization. Significant savings of almost €600 were only achieved in study arm II according to German prices.

CONCLUSION

With proper patient selection, a gradual approach with the Enteer® as the primarily used device, with the Outback® used additionally in case of failure, leads to significant savings and can be recommended. In severe calcification, the Outback® should be used as the primary device.

KEYWORDS

Outback®, Enteer®, OffRoad®, re-entry device, economic evaluation, subintimal angioplasty, femoro-popliteal, chronic total occlusion

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The number of patients requiring interventional treatment for symptomatic peripheral artery disease (PAD) has been rising continuously over recent years.[1] Therefore, a large number of angioplasties for the treatment of chronic total occlusions (CTO) end up being subintimal revascularizations. In about 20% of all subintimal recanalizations of femoro-popliteal arteries, spontaneous re-entry into the true lumen distally to the CTO may fail and thus jeopardizes a successful revascularization.[2] As well as retrograde access, re-entry catheters have shown to be helpful in this regard.[3,4] The high acquisition costs, however, deter many potential users. But ultimately, an unsuccessful, aborted recanalization with a subsequent second attempt or bypass surgery is more expensive for the healthcare system than the use of a re-entry device in selected cases. In this regard, the Outback® catheter (Cordis – a Cardinal Health company, Santa Clara, CA, USA) has been the first available system on the market since 2003, and there are several studies on femoro-popliteal subintimal revascularization confirming a technical success rate clearly exceeding 90%.[4,5] In 2012, the Enteer® catheter (Medtronic, Minneapolis, MN, USA) was released with a published success rate of 86%.[6] Finally, in 2013, the OffRoad® catheter (Boston Scientific, Marlborough, MA, USA) followed with a technical success rate of 84.8%.[7] These three conventional re-entry devices differ much greater in their acquisition costs than in their stated effectiveness, implying a great potential for savings. So far, there are no studies comparing the potential economic savings of the catheters, as well as their technical efficiency and limitations in this regard.

Methods

The institutional review board approved the conduction of this study and the subsequent analysis of anonymized patient data (BKF-A-2018-11) and waived the need for informed consent. The study was performed concordantly with the ethical standards of the 1946 Declaration of Helsinki and its later amendments.

Main points

- When primarily using the Enteer® catheter for device-assisted re-entry in femoro-popliteal occlusions, a relevant and significant cost reduction can be achieved per patient.
- When treating heavily calcified re-entry sites, the Outback® device has a clear advantage over the other tested re-entry devices.
- For a large distance to the true lumen due to a wide dissection, all tested re-entry devices show distinct weaknesses and should be omitted.

Introduction of the devices

The OffRoad® system consists of a 6F catheter with a pear-shaped 5.4 mm positioning balloon at the tip for alignment within the dissection and direction of the tip towards the true lumen. A separately supplied microcatheter lancet with a narrow lumen sufficient for a 0.014" wire is inserted coaxially. The balloon catheter can be guided to the target position via a 0.035" wire. However, the exceptionally poor crossing profile at the catheter tip regularly necessitates pre-dilation of the passed occlusion. After positioning the catheter tip in the desired position and inflation of the balloon, the puncture is made with the lancet, and finally, the further course of the vessel is probed with the 0.014" wire. The needle can be bent slightly at the tip for better targeting.

In contrast to this, the Enteer® device is advanced over 0.014" or 0.018" wires. The crossing profile is comparable to standard 0.018" balloons and thus optimal for the passage of even long, complex occlusions regularly without pre-dilation. The distal end of the catheter is positioned within the dissection parallel to the target lumen. After the inflation of the flat-shaped balloon at the tip of the catheter for its self-orientation, re-entry ensues using the 0.018" Enteer® guidewire. Its short, angled tip allows the selection of the appropriate side hole on the side of the balloon facing the true lumen. The guidewire is available in three degrees of stiffness (flexible, standard, and stiff). During this study, we regularly used the stiff guidewire for penetrating the dissection membrane.

The Outback® catheter is advanced to the desired re-entry site using a 0.014" wire. Due to the adequately shaped profile and the stiff catheter shaft, the catheter can usually be advanced without pre-dilation. Positioned parallel to the true lumen, the catheter tip is correctly aligned under fluoroscopy at two projection angles, once with the catheter in overlay with the target vessel and once with the catheter and target vessel exactly parallel to each other. A needle is then deployed laterally, and the target lumen is punctured. This system offers the best direct control of the direction of puncture. However, the Outback® catheter shows a clear disadvantage for crossover maneuvers in steep aortic bifurcations due to its rigid catheter, which either tends to break in extreme cases just below the stiff deployment site of the needle (Outback® Elite) or is just not able to cross the bifurcation (Outback® LTD). This restriction has already been detailed by Raskin et al.[8]

All procedures were performed by one of three experienced interventionalists with at least six successful applications of the Outback® catheter in femoro-popliteal CTO. Prior to the first use of the OffRoad® and the Enteer® device in the context of this study, all interventionalists were instructed by a product specialist, and the first three applications for each device were performed in the presence of at least two of the interventionalists. No initial application was carried out by a sole individual.

Economic considerations

The potential economic savings for the initial application of either the OffRoad® or the Enteer® device in contrast to the solitary utilization of the Outback® catheter were calculated. Since the economic break-even point depends on the prices, the formula »*price of competitor * 100/price of Outback®*« can be used to calculate the needed success rate for the economically sensible use of different devices. When using the offered prices in Germany (Outback®, €1,700; OffRoad®, €795; Enteer®, €540; all before tax), the break-even point for the Enteer® device equates to a success rate of 32%, while the OffRoad® needs a success rate of 47%. With published technical success rates beyond 80%, relevant savings should be achievable with both systems.

Retrospective evaluation

The prospective observational study was preceded by a retrospective evaluation of the experience with the Outback®. All consecutive patients who had ever been treated with the Outback® re-entry device in the setting of percutaneous subintimal recanalization of femoro-popliteal CTO since its introduction to this tertiary hospital in December 2015 were included. For every patient, the demographic baseline data, lesion characteristics, and technical success rate of the device were noted.

Prospective analysis

The prospective observational part of the study started in June 2018 and lasted until January 2020. In those 20 months, all consecutive patients presenting with a femoro-popliteal CTO, who were treated with a percutaneous subintimal recanalization, were included, whether or not a re-entry catheter was used. No hybrid procedures were included. The exclusion criteria were luminal pas-

sage of the occlusion, previous interventions with the necessity of femoro-popliteal placement of stents or stent grafts, or any previous angioplasty of the target lesion within the three months before the index procedure. Acute or subacute occlusion with a sudden onset of symptoms consistent with arterial thrombosis or thromboembolism were also excluded. Except for these exclusions, all consecutive interventions were included and documented in detail. In the case of unsuccessful primary re-entry with the standard wire techniques, a re-entry device was used in the distal femoral or popliteal artery. For the first 20 patients (study arm I), the OffRoad® catheter was used, while the following 20 patients (study arm II) were treated with the Enteer® catheter. In the case of failure of assisted re-entry, the Outback® catheter was employed as a bailout. The patient collection started with the first OffRoad® device being used and was completed after the inclusion of the twentieth patient being treated with the Enteer® re-entry device. Figure 1 illustrates the course of the study as a flowchart.

Baseline and procedural characteristics

For all patients, demographic baseline data, relevant comorbidities, and clinical stage of PAD according to the Rutherford classification were documented. In addition, lesion characteristics such as location; length; the degree of calcification documented as none, mild (<25% circumference), moderate (25%–50%), or severe (>50%); the level of re-entry to the true lumen; and the time until spontaneous re-entry were noted.[9] The technical success of the re-entry maneuver itself, either with or without a re-entry device, as well as the overall procedural success defined as successful target vessel recanalization, were documented. Furthermore, in the case of an assisted re-entry, the time until successful re-entry was noted (time from insertion of the device until successful access to the true lumen with the 0.014" wire in minutes). Subgroup analyses were performed after excluding patients in whom a re-entry catheter was foreseen to fail before use and in all patients with severe re-entry site calcification. Device-related complications were documented and classified according to the Society of Interventional Radiology Classification System for Complications by Outcome.

Procedure

All procedures were performed in a standard angiography suite using a Philips Allura Xper FD20 angiography system (Philips Healthcare, Best, The Netherlands). All procedures were conducted percutaneously. Whenever possible, an antegrade approach via the ipsilateral common femoral artery was chosen with the placement of a 6 or 7 French sheath. If an antegrade approach was not possible due to obesity or a proximal start of the occlusion, a retrograde approach via the contralateral common femoral artery and subsequent crossover maneuver was chosen. A 45 cm long, 6 French Destination® (Terumo Corporation, Tokyo, Japan) or Fortress® (Biotronik, Berlin, Germany) sheath was introduced and used as access to the target lesion.

Under roadmap guidance, subintimal probing of the occluded vessel segment was performed using either a diagnostic catheter with a short angled tip (Cordis® Tempo® Vertebral Catheter, Cordis, a Cardinal Health Company, Santa Clara, CA, USA) in combination with a 0.035" hydrophilic guidewire (Radiofocus® Guidewire M Standard Type, Terumo Corporation, Tokyo, Japan) or a low-profile support catheter (0.018" TrailBlazer™, Medtronic, Minneapolis, MN, USA) combined with a 0.018" CTO wire (Hi-Torque Command ES guidewire, Abbott, Chicago, IL, USA). The time after passage of the CTO, either until successful spontaneous re-entry or until the decision to introduce a re-entry device, was noted. In the first 20 patients, the OffRoad® catheter was used, and in the following 20 patients, the Enteer® catheter was used. In a case of failed assisted re-entry with either of these systems, the Outback® catheter was used as a bailout tool.

After successful re-entry balloon angioplasty and in the case of residual stenosis due to dissection, recoil, or heavy calcification, self-expandable nitinol stents or stent grafts (Innova®, Boston Scientific, Marlborough, MA, USA; GORE® VIABAHN® and TIGRIS®, W. L. Gore & Associates, Inc., Newark, DE, USA; Supera®, Abbott Vascular, Santa Clara, CA, USA; Astron Pulsar®, Biotronik, Berlin, Germany) were deployed to secure the result. The number of stents and stent grafts used to treat the lesion was documented.

Statistical analysis

Demographic and clinical baseline data are presented as means with corresponding standard deviations (SD) for metric variables and with absolute counts and percentages for nominal variables. Baseline variables were compared between the retrospective and the prospective cohort as well as between the two study arms using the t-test for unpaired samples for all metric variables and the chi-square test for nominal variables. For the latter, categories of lesion and re-entry site calcification were simplified to none, mild, and moderate vs. severe. The performance of the two OffRoad® and Enteer® re-entry devices was compared with the overall performance of the study arm determined by the combined success rate of the Outback® or the Enteer® device and the occasionally necessary subsequent use of the Outback® catheter. The chi-square test was used for this purpose. The cost–benefit of the primary use of either of the two systems studied was then investigated. The actual additional per-patient costs caused by using one or two re-entry devices were compared with the fictitious costs that would have been incurred by the primary and sole use of the more expensive

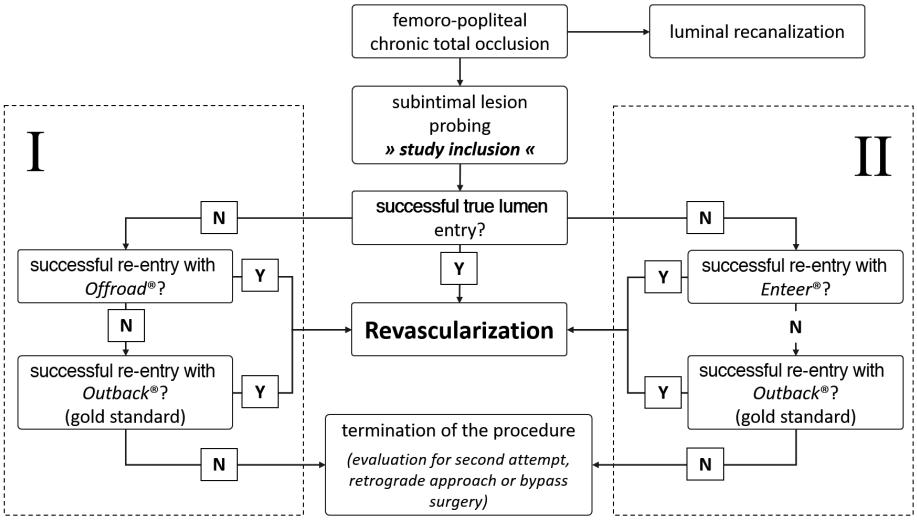

Figure 1. Illustration of the course of the prospective block-randomized study with the OffRoad® catheter used in study arm I and the Enteer® catheter used in study arm II. Each study arm includes 20 lesions that required the use of a corresponding re-entry device. Y, yes; N, no.

Outback® device. The comparison was made using the Mann–Whitney U test.

Results

Retrospective analysis

Since its introduction in our clinic in December 2015 and before the start of the prospective study in June 2018, 31 lesions in 31 patients were treated with the Outback® device during subintimal revascularization of femoro-popliteal CTO. Table 1 shows the demographic baseline data and lesion characteristics for the included patients. The deployment of the Outback® re-entry device was successful in 30 patients, resulting in a technical success rate of 97%. This justified its definition as a gold standard in the context of this study.

Prospective analysis

Table 1 offers basic demographic data for all enrolled patients as well as for each study arm separately. There were no statistically significant differences between the retrospective and prospective cohort in general in terms of patient age, lesion length, and lesion, as well as re-entry site calcification. However, in the prospective cohort, target lesion and re-entry site calcifications were significantly more often severe in the study arms, necessitating the use of re-entry catheters compared to those patients with spontaneous re-entry ($P < 0.010$).

An unassisted re-entry could be achieved in 68 of 109 treatments, which amounts to a primary procedural success rate of 63%. The average time until spontaneous re-entry was 1.7 min (SD: 5.1). In one case, the passage of the chronic artery occlusion was not possible due to massive calcification and was counted as primary procedural failure (0.9%). We deemed spontaneous re-entry a failure after an average of 6.7 min (SD: 5.6) of probing and proceeded with the use of a re-entry device.

Figure 2 offers an overview of the results regarding the technical and procedural success. The OffRoad® was successfully deployed in 9/20 (45%) cases with an average time until successful re-entry of 12.5 min (SD: 6.4). In the case of failure of the OffRoad®, the Outback® catheter ensured success in another 8/10 (80%) procedures after a mean total time from the use of the first device until re-entry of 15.2 min (SD: 12.9). During one procedure, re-entry was achieved spontaneously further distal from the originally chosen re-entry site after an unsuccessful attempt with the OffRoad® device and before using the Outback® catheter according to the study protocol. The Enteer® re-entry device was successfully used in 12/20 (60%) patients. Another 5/8 (63%) re-entries could be achieved by the usage of the Outback® catheter. The average time until successful re-entry was 6.65 min (SD: 6.4) for the Enteer® catheter and 8.25 min (SD: 12.9) when the additional use of the Outback® catheter was necessary. The technical success rate for the OffRoad® catheter was significantly worse than the overall performance after additional use of the Outback® catheter in study arm I ($P = 0.003$). The success rate of the Enteer® catheter only narrowly missed that significance level in study arm II ($P = 0.077$).

Table 1. Demographic baseline data

		Retrospective cohort	Prospective cohort				*P* values*
		Outback®	Complete cohort	Spontaneous re-entry	Study arm I (OffRoad®)	Study arm II (Enteer®)	
Number of patients		31	99	60	19	20	-
Number of lesions		31	109	69	20	20	-
Age in years given as mean (SD)		75 (9.1)	74.2 (9.7)	73.1 (9.7)	74.6 (10.1)	74.2 (9.3)	0.674/0.207
Sex (M:F)		15:16	67:32	49:20	13:7	11:9	0.052/0.519
Rutherford stage		-	-	-	-	-	0.522/0.381
	1	0 (0)	1 (1)	1 (1.5)	0 (0)	0 (0)	-
	2	2 (7)	2 (2)	1 (1.5)	0 (0)	1 (5)	-
	3	13 (42)	36 (33)	25 (36)	8 (40)	3 (15)	-
	4	3 (11)	15 (14)	9 (13)	3 (15)	3 (15)	-
	5	10 (33)	40 (36)	24 (35)	7 (35)	9 (55)	-
	6	2 (7)	15 (14)	9 (13)	2 (10)	4 (20)	-
Lesion length (cm) given as mean (SD)		17.5 (9.5)	18.1 (10.7)	17.4 (10.6)	16.9 (9.2)	19.9 (12.1)	0.815/0.361
Target lesion calcification		-	-	-	-	-	0.120/0.197
None		5 (16)	25 (23)	18 (26)	3 (15)	4 (20)	-
	Mild	13 (42)	28 (26)	27 (39)	1 (5)	0 (0)	-
	Moderate	7 (23)	19 (17)	10 (15)	6 (30)	2 (10)	-
	Severe	6 (19)	37 (34)	14 (20)	10 (50)	14 (70)	-
Calcification of re-entry site		-	-	-			0.883/1
None		6 (19)	27 (25)	20 (29)	3 (15)	4 (20)	-
	Mild	14 (45)	31 (28)	27 (39)	2 (10)	2 (10)	-
	Moderate	4 (13)	25 (23)	13 (19)	6 (30)	5 (25)	-
	Severe	7 (23)	26 (24)	9 (13)	9 (45)	9 (45)	-

*P values for the statistical significance testing for "retrospective collective vs. complete prospective collective" / "study arm I vs. study arm II". SD, standard deviation; M, male; F, female.

When analyzing possible causes of device failure, three cases were clearly due to a wide dissection, resulting in a great distance between the true lumen and the re-entry device. Retrospectively, these cases were highly unlikely to be successful from the outset, and the primary omission of a re-entry device would have been legitimate. However, according to the study protocol, the devices were used regardless of the probable failure to avoid selection bias. A subgroup analysis with exclusion of these three cases revealed the results presented in Figure 3. With this clinically justifiable modification, not only was the technical success rate of the OffRoad® catheter significantly worse than the overall re-entry device performance in study arm I ($P = 0.001$) but it was also now worse than the rate of the Enteer® catheter in study arm II ($P = 0.035$).

The success rate of the Outback® device as a backup tool in the prospective study arms was 13/18 (72%) for the entire study population and 13/15 (87%) in the reduced cohort, according to Figure 3. In conjunction with the success rate in the retrospective part of the study, this results in an overall technical success rate of 43/49 (88%) and 43/46 (93%), respectively.

Another subgroup analysis was introduced to examine possible differences in spontaneous and device-assisted re-entry in severely calcified vessels. Table 2 shows the cases of severely calcified re-entry sites with the exclusion of the above-mentioned predictable failures and their success rates.

After the successful passage of the target lesion, subsequent angioplasty in all and additional stent/stent-graft placement in 94/109 (86%) lesions were conducted. On average, 1.7 (SD: 0.8) stents or stent grafts were used for treating the target lesion. Considering all prospectively enrolled patients, the overall procedural success rate equates to 95% (103/109).

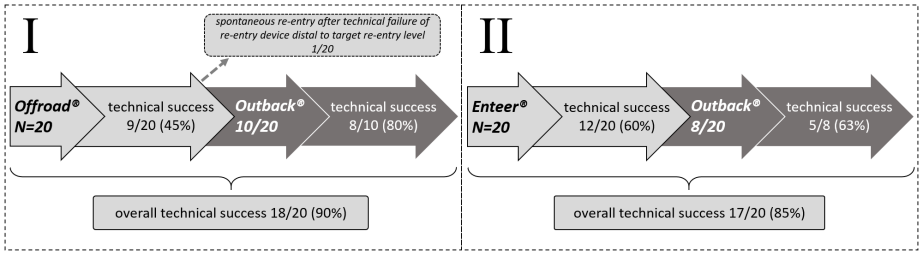

Figure 2. Overview of the technical success rates of the used devices in the two sequentially arranged study arms.

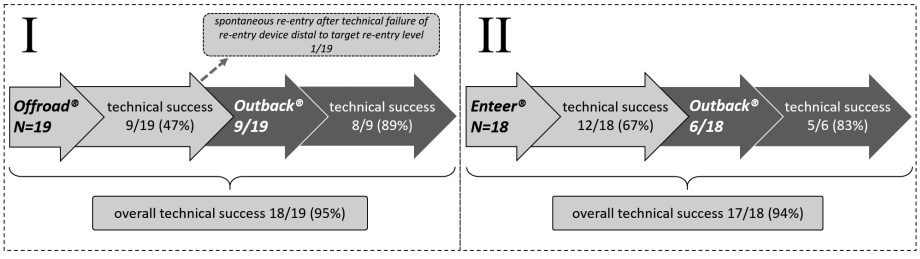

Figure 3. Overview of the technical success rates of the used devices in the two sequentially arranged study arms in a subgroup analysis with the exclusion of three cases with predictable device failure due to a wide distance between the true lumen and the re-entry device.

Economic evaluation

The additional costs resulting from the use of one or two re-entry catheters were calculated separately for each study arm. The additional costs in study arm I could amount to €795 for the sole use of the OffRoad® device or €2.495 (795 + 1.700) in the case of the additional necessary use of the Outback® catheter. Similarly, additional costs in study arm II amounted to €540 or €2.240 (540 + 1.700). This also explains the wide range of SDs. The statistically insignificant mean reduction of per-patient costs for each study arm was €55 (SD: 850) (3%) for the OffRoad® and €480 (SD: 833) (28%) for the Enteer® device. When excluding the three cases with predictable technical failure, the per-patient cost reduction rose to €100 (SD: 849) (6%) for the OffRoad® and €593 (SD: 801) (35%) for the Enteer® device, the latter now reaching significance ($P = 0.036$) despite the fact that the success rate of the Enteer® device was significantly inferior to the overall re-entry device performance with the help of the Outback® catheter.

Discussion

The major perspective of this study was the comparison of re-entry devices to evaluate possible economic savings. However, the actual calculated savings were much lower than anticipated. When looking at the literature, the performance of both prospectively compared re-entry devices should have been better, resulting in a considerably larger effect size when looking at the potentially saved costs. With a success rate of 93%–96% for the Outback® catheter, 84.5% for the OffRoad® catheter,[7] and 86% for the Enteer® catheter[10] and vastly different acquisition prices, the number of patients needed to demonstrate significant economic savings in the chosen study design were expected to be low. This partly explains the small number of patients planned for the analysis. However, despite the surprisingly low success rate of the two compared devices, a significant

Table 2. Subgroup "severely calcified re-entry sites"

Subgroup "severely calcified re-entry sites"		Number of patients	Success rate	Additional use of the Outback®	Success of the secondary Outback®
Retrospective cohort (Outback®) (%)		7	7/7 (100)	-	-
Prospective cohort (%)					
	Complete collective	24	14/24 (58)	10	9/10 (90)
	Spontaneous re-entry	9	9/24 (38)	-	-
	Study arm I (OffRoad®)	8	3/8 (38)	5	5/5 (100)
	Study arm II (Enteer®)	7	2/7 (29)	5	4/5 (80)

reduction in costs could only be achieved by primarily using the Enteer® device and the Outback® catheter as a bailout device after excluding three cases with anticipated failure due to a large distance between the device and the target vessel lumen.

In addition, the chosen low number of patients per study arm seemed appropriate, as we did not expect a long initial training period since fast and intuitive handling for those rarely used devices is essential. Therefore, it is important that every interventionalist can successfully employ them after a short training interval in the femoro-popliteal segment. Other locations, such as the tibio-peroneal arteries, certainly require more experience.[11,12] Furthermore, the initial training period for the gold standard, the Outback® catheter, was also included in this study to facilitate the comparison between the re-entry devices. To minimize the effect of three separate learning curves in three interventionalists, all were instructed beforehand by a product specialist and were able to test the systems *in vitro*. The first applications were then always conducted in a team until everyone was aware of the individual advantages and disadvantages of the systems and could work quickly with the same level of experience.

With a success rate of only 45%, this study showed a considerably lower success rate for the OffRoad® catheter than that by Schmidt et al.[7] However, Schmidt et al.[7] did exclude almost all patients with severe calcification of the target lesion from the study, resulting in a rate of severe calcifications of only 5.4%. For those few included cases with severe calcification, a success rate of only 60% was documented, while cases with mild calcifications showed a success rate of 93%. Moreover, the OffRoad® catheter was used primarily without previously trying to achieve a spontaneous re-entry, which is a rather unusual study design for such a device. With an average time until re-entry of 11.1 min (SD: 10.5), this time is comparable to that in our study (12.5 min; SD: 6.4). Finally, it should be mentioned that the study was not conducted independently of the manufacturer, which may explain the deficiencies in the study design and the interpretation of the results. The first study of this device in humans, with the inclusion of just six patients, indicated a success rate of 83% when using the OffRoad® catheter after failed primary revascularization, even in cases of severe calcification.[13] We were not able to reproduce this success rate.

One big advantage of the Enteer® catheter, in contrast to the OffRoad® device, is its sleek crossing profile. A passage to the desired re-entry site can be achieved without issue. The comparably much shorter time until re-entry of only 6.65 min vs. 12.5 min with the OffRoad® device reflects this. However, the maximum 67% success rate of the Enteer® device shown in this study was much lower than in the peripheral facilitated antegrade steering technique-CTO trial, where a success rate of 86% for the Enteer® catheter after failed primary recanalization was documented.[10] There, the re-entry device was used in 21 out of 66 cases. The exact lesion characteristics were not described, but only in 45% of the 66 patients were the vessels described as moderately or severely calcified. In our study, 16 out of 20 target lesions (80%) were at least moderately calcified. This may explain the lower success rate and also emphasize the necessity of careful consideration of the chosen re-entry device. Ultimately, the Enteer® catheter failed to achieve the expected technical success rate in the present study. However, when excluding patients with expected failure of the device due to a large distance between the device and the true lumen, the calculated economic savings per patient of almost €600 were significant and relevant.

When comparing the group with spontaneous re-entry to those with the need for re-entry devices, the impact of re-entry site calcification becomes obvious. Only 13% (9/69) of re-entry sites were severely calcified in the group with spontaneous re-entry. On the other hand, 45% (18/40) of re-entry sites in study arms I and II were severely calcified. Hence, the grade of calcification can be used as a predictor for the necessity of a re-entry device. The Enteer® catheter also revealed its greatest weakness in the presence of severe calcification, with an associated technical success rate of only 29%. Contrary to the results of Shin et al.[14], the Outback® device showed excellent results even in the severely calcified re-entry sites with a success rate of 90% (25/27). Thus, the extent of calcification of the re-entry site can certainly be used as an additional selection criterion, with the Outback® favored over the Enteer® catheter in such cases. Hence, it should be possible to achieve an even greater cost advantage. In our study, the Outback® device proved its great performance despite being used only in difficult cases when the other re-entry devices had failed. With a retrospective success rate of 97% (30/31) and a success rate of up to 87% (13/15) in the prospective study as a bail out, the overall success rate of the Outback® catheter was 93% (43/46). This concurs with other studies.[5,15,16] Hence, the definition as a gold standard was justified. As already described in previous studies, possible predictors of failed assisted re-entries were heavy calcification with consecutive difficulty tracking the device over the wire or an acute angle of the aortic bifurcation in crossover recanalization.[8,14] However, in the majority of cases, it impresses with its very easy and swift application, which was proven by the documented re-entry times when used as a bail out. When using the OffRoad® device, a re-entry time of 12.5 min (SD: 6.4) was documented. However, if it failed, the combined time until re-entry with the additionally used Outback® device took, on average, no more than three minutes longer (15.2 min; SD: 12.9). The same was shown for the Enteer® device. By itself, a time of 6.65 min (SD: 6.4) until re-entry was documented, and in the case of failure, the entire re-entry time with the additionally used Outback® catheter was only two minutes greater (8.25 min; SD: 12.9).

The primary procedural success rate without a re-entry device in this study was 63%. Other studies have shown a higher primary success rate between 80% and 92%.[2] In this meta-analysis, lesion characteristics and the exact procedural events were not mentioned and, therefore, cannot be compared to our study. Since we started including patients with the use of the first re-entry device and closed the acquisition with the use of the fortieth re-entry device, we artificially distorted the actual primary success rate. Furthermore, we placed a great deal of importance on a targeted re-entry, which prevented us from using aggressive wire maneuvers to ensure re-entry. Moreover, we refrained from using any additional auxiliaries, such as the subintimal application of balloons to achieve re-entry, to keep the subintimal space as narrow as possible and, thus, the starting conditions for the devices as comparable as possible. In the context of this study, we also refrained from using a retrograde access to the lesion, which is, of course, a viable and cheap, but no less complex, alternative.[17] The learning curve for the distal retrograde access (either pedal, tibio-peroneal, or popliteal) and for the corresponding access site management is longer than for the application of the Outback® catheter, and the possible complications of the additional access site could be much more serious, especially when considering the popliteal artery. We, therefore, never use this approach in claudicants and think that re-entry devices

are an ideal tool to deal with these situations via a single access route. For the purpose of the study, we have generally avoided this technique. Another very exciting application is the retrograde insertion of the Outback® catheter in lesions that cannot be treated in any other way.[18] With growing experience and confidence in the use of retrograde access and the Outback® catheter, this option can be a game changer in selected cases.

The selection of devices used in our study was based on the great difference in their acquisition costs in comparison to the Outback® device and, thus, the potential for economic savings. The Pioneer Plus® re-entry device would have been a possible alternative as a gold standard. However, a lack of experience with this device prevented its use in our study. Furthermore, despite comparable acquisition costs for the Pioneer Plus® and the Outback® catheter, the additional need for an intravascular ultrasound system for the Pioneer Plus® may imply an additional hurdle for most users. Moreover, its use is usually reserved for more complex applications.[19] For this study, selected off-the-shelf devices can all be applied without additional equipment, with the exception of the guidewires, and can thus be implemented in the daily routine without problems.

A recently introduced device is the GoBack® catheter (UPSTREAM Peripheral Technologies Ltd., Israel). However, the cost of this re-entry device is comparable to the Outback® catheter. Its use suggests no possibility of economic savings, so we excluded it from this study. A prospective head-to-head comparison with the Outback® catheter would be a useful study. However, the GoBack® catheter is being promoted with the additional characteristic of a crossing device, which differs greatly from the included devices in this study. To compare such vastly different devices in the setting of this study would have been problematic. Nevertheless, in this study, there was only one case in which the passage of the target lesions was not possible using the standard guidewire technique. So, the number of cases in which the promoted characteristic of a crossing device of the GoBack® catheter being an advantage seems to be limited.

The main limitations of the present work are the comparatively small number of patients per study arm, which has already been discussed, but also the lack of clinical follow-up of the patients. However, this seemed irrelevant to the study objective. Clinical success and value of femoro-popliteal recanalizations in symptomatic PAD, as well as the value of subintimal recanalization, have been sufficiently investigated in larger cohorts.[20] Our study would not have contributed any decisive added value, and this information would have merely overloaded the manuscript.

In conclusion, due to its low success rate, the OffRoad® re-entry device offers no options for cost savings. The Enteer® catheter, in contrast, seems to offer the possibility of significant savings in a gradual approach with the Enteer® catheter as the primarily used device and the Outback® catheter only utilized in the case of failure of the Enteer®. Predictable failures for any device result from too great a distance between the device and the target lumen in a wide dissection. In these cases, the additional use of a re-entry device and the associated costs can be omitted. In cases of severely calcified re-entry sites, the primary use of the Enteer® device cannot be recommended. In these cases, the primary use of the Outback® catheter offers higher chances of success. Thus, the significant average savings per patient documented in this study may even be exceeded.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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