Original research

Evaluation of a novel flow diverter, the DiVeRt system, in an animal model

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/neurintsurg-2021-017430).

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Received 15 February 2021
Revised 29 April 2021
Accepted 3 May 2021

To cite: Hufnagl C, Broussalis E, Cognard C, *et al*. *J NeuroIntervent Surg* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/neurintsurg-2021-017430

ABSTRACT

Background Using a surgical aneurysm model, this study assessed the performance of a new flow diverter (FD), the DiVeRt, and evaluated the angiographic and histologic features at different periods after stent deployment.

Methods Fifteen New Zealand White rabbits were treated 3 days prior to intervention and until euthanization with dual antiplatelets. DiVeRt was implanted in bilateral carotid aneurysms (n=30) as well as in the aorta (n=15). The rate of technical success, assessment of aneurysm occlusion (measured by the O'Kelly–Marotta grading (OKM) scale), and stent patency were examined using angiography and histologic examinations in three groups at 1, 3, and 6 months follow-up (FU). In each FU group one control animal was included and treated with the XCalibur stent (n=3).

Results Overall, DiVeRt placement was successful and without apparent intraprocedural complications. In total, four stents in the carotid artery were occluded and in-stent stenosis was registered in two carotid (7%) and one aortic (6%) vessels. Complete or near complete aneurysm occlusion (OKM scale D1 and C3) was seen in 100% in the 1-month FU group, 70% in the 2-month FU group, and 100% in the 3-month FU group. Histology showed loose, organizing fibrous tissue matrix within the sac and adequate neck endothelialization in all vessels. All branches covered by the DiVeRt remained patent.

Conclusions The DiVeRt system appears to be feasible and effective for the treatment of aneurysms with high rates of complete aneurysm occlusion, excellent vessel patency, and evidence of high biocompatibility. Occurrences of parent artery occlusion at follow-up did not result in clinical consequences.

INTRODUCTION

Endovascular treatments for intracranial aneurysms have evolved significantly and allow for the treatment of even complex aneurysms.[1–3] It remains challenging, however, to achieve cure of certain complex aneurysms. Advances in knowledge and understanding of hemodynamic and morphological characteristics of aneurysms have led to continuous improvement regarding the design of embolization devices. Flow diverters (FDs) aid with vascular reconstructive processes of the parent artery, which lead to aneurysm occlusion over time due to intra-aneurysmal thrombosis and aneurysmal neck endothelialization.[3–5] They provide a scaffold for endothelial cells to grow while maintaining vessel patency.[6] Various FDs are currently available that have proven safety and efficacy in clinical practice.[7] The DiVeRt (Device for Vascular Reconstruction; Merlin MD Pte Ltd, Admirax, Singapore) is a newly designed FD. This preclinical study in a rabbit aneurysm model was performed to analyze the safety and efficacy of this new FD.

METHODS

Device

The DiVeRt stent has a laser-cut nitinol structure, cut into a cylindrical stent shape and sandwiched in a microporous polymer membrane that forms the working zone. The polyurethane (polymer) membrane goes through a proprietary surface modification process which results in a highly hydrophobic luminal surface and hydrophilic abluminal surface. Thus, the luminal surface has very low thrombogenicity and provides the critical surface tension that prevents thrombus from attaching and propagating. The polymer membrane may also exhibit excellent biocompatibility and biostability. Three radiopaque markers are attached at each end of the implant and the working zone is visible via radiopaque ring markers. The implant is coated with the aforementioned proprietary polymer with specific surface characteristics for about 80% of the total length, leaving about 20% of the length uncoated on the proximal and distal ends of the implant. The polymer membrane on the working length is laser drilled to provide 50–60% surface coverage. The implant is then loaded onto a custom transport wire into a transport sheath (figure 1A). This transport sheath just constrains the implant until it is loaded into the microcatheter, to be pushed out to the implant site during the procedure.

In the control animals, the XCalibur system (Merlin MD Pte Ltd), a laser-cut stainless steel implant sandwiched in a similar although thicker microporous polymer membrane pre-mounted on a 6Fr balloon catheter with flow diversion effect, was implemented.[8]

Surgical aneurysms in a rabbit model

All animal procedures were performed in accordance with the Austrian regulations and guidelines governing animal experiments. Following approval from the Committee of Animal Experiments of the federal province Salzburg, Austria, sidewall

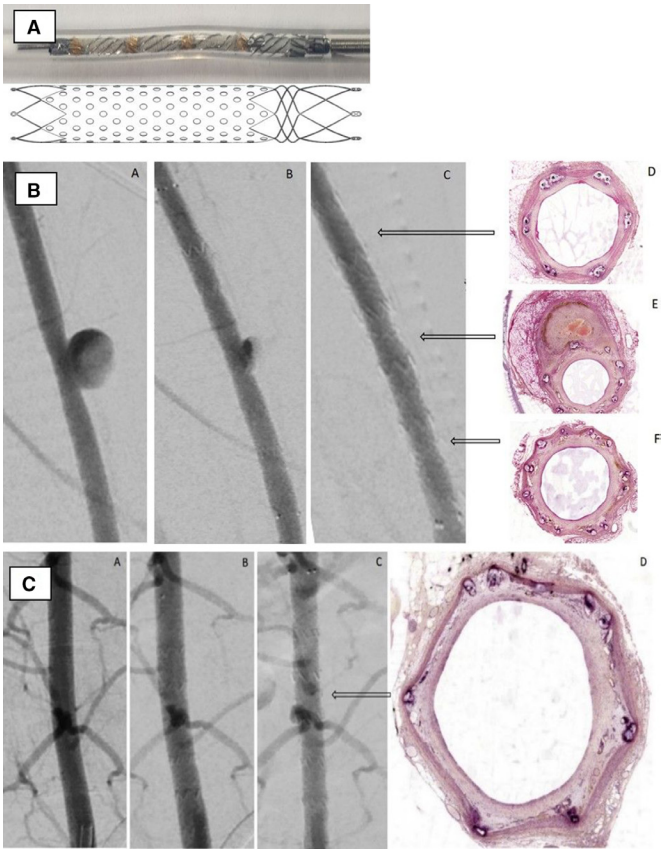

Figure 1 (A) Original and schematic illustration of the DiVeRt flow diverter system with a laser-cut nitinol structure in a microporous polymer membrane that forms the working zone. Three radiopaque markers are attached at each end of the implant and the working zone is radio visible via regularly spaced radiopaque ring markers. The figure shows a 4 mm diameter implant with a 18 mm working length. (B) Animal 2018: angiographic and histological imaging of the vessels. A: carotid artery including the aneurysm before treatment; B: carotid artery after flow diverter implantation; C: end angiography after 90 days; D: histological analysis of the distal part of the carotid artery with implanted stent (light microscopy examination; hematoxylin and eosin stain); E: histological analysis of the middle part of the carotid artery with implanted stent at the site of the aneurysm neck; F: histological analysis of the proximal part of the carotid artery with implanted stent. (C) Animal 12217: angiographic and histological imaging of the vessel. A: aorta before treatment; B: aorta after flow diverter implantation; C: end angiography after 180 days; D: histological analysis of the middle part of the aorta with implanted stent (light microscopy examination; hematoxylin and eosin stain).

aneurysms were created in both common carotid arteries in 15 New Zealand White rabbits; three further animals were used for controls. Selected animals weighed 2.6–3.5 kg. Performance was in accordance with the standards of the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines.[9]

Details of the creation procedure have been published previously.[10] Anesthesia was induced by subcutaneous injection of ketamine (75 mg/kg) and xylazine (4 mg/kg), followed by maintenance anesthesia by intravenous injection of a saline solution of ketamine and xylazine (5:1:5; 0.5–1 mL/hour/kg). Throughout the procedure the animals were breathing spontaneously and the anesthetic agent was administered via the lateral auricular vein.[11] All rabbits received antibiotic prophylaxis and analgesia by subcutaneous injection of enrofloxacin (7.5 mg/kg) and meloxicam (0.3 mg/kg) on the day of the procedure. Daily antibiotic and analgesic therapy were continued for 5 days following surgery. Aspirin (10 mg/kg) and clopidogrel (10 mg/kg) were given daily for 3 days before implantation and were continued for 30 days after treatment in all animals. For all angiographies, non-ionic iodinated contrast media (300 mg iodine/mL) was used.

Endovascular treatment

Three weeks after surgery the patency of all the aneurysms and parent arteries was confirmed by DSA prior to DiVeRt deployment. Under fluoroscopic guidance, a 6Fr introducer sheath was inserted into the femoral artery. Briefly, a 6Fr sheath was advanced on one side of the femoral artery via cut down, followed by a 6Fr commercially available guiding catheter. A 0.028 inch microcatheter was advanced into the target artery over a 0.014 inch microwire through the guiding catheter.

The DiVeRt stents were first deployed across the aneurysm neck within the right and left carotid arteries (sizes were chosen in accordance with vessel diameter: either 18 mm/15 mm or 18 mm/18 mm). The third device was deployed within the infrarenal aorta crossing multiple lumbar arteries (sizes were chosen in accordance with the aortic diameter: either 3.8 mm/15 mm or 5.0 mm/22 mm). DSA was performed through the guiding catheter immediately after deployment.

At the end of the procedure all catheters were removed. The femoral artery was ligated proximal to the arteriotomy site. The skin incision was closed with Vicryl suturing (Ethicon). All animals were monitored during and after the procedure.

Study design

The study included a total of 18 animals. In 15 animals, each carotid aneurysm (left and right, n=30) as well as the infrarenal aorta (n=15) were treated with the DiVeRt system. For control, the XCalibur stent was implanted in the right carotid artery of three animals, of which two had a sidewall aneurysm (n=3).

The animals were divided into three follow-up (FU) groups comprising six animals each. Of these, five were treated with DiVeRt and one with XCalibur. Animals in the 1-month FU group had end angiography at 1 month, animals in the 2-month FU group had control angiography at 1 month and end angiography at 3 months, and animals in the 3-month FU group had control angiography at 3 months and end angiography at 6 months. The characteristics of the devices were evaluated according to usability, performance, and safety endpoints.

Animals were sacrificed with a lethal injection of embutramid-mebezoniumiodid-tetracain solution (1 mL/kg body weight) at each time point after the last DSA follow-up.

Degrees of intra-aneurysmal flow disruption immediately after device deployment, at control angiography and before sacrifice were graded in accordance with the O'Kelly–Marotta (OKM) grading scale.[12] The patency of the parent artery and lumbar artery branches was also evaluated.

Histopathology

Carotid arteries, including the aneurysm sac and aortic segment with lumbar arteries, were immediately fixed in 4.5% neutral buffered formalin and submitted for histological processing to LLS Rowiak LaserLabSolutions GmbH (Hannover, Germany). All sections containing the aneurysm sac and neck were evaluated by light microscopy to score histologic changes on the basis of a semi-quantitative grading scale. The histologic rating was graded from none (0) to minimal (1), mild (2), moderate

(3), and marked (4). Semiquantitative morphologic changes were rated according to platelet/thrombus formation, endothelialization, and neointima formation in the aneurysm neck and intraluminal organization, inflammation, and neoangiogenesis in the aneurysm sac. The inflammation was graded as minimal (≤20 inflammatory cells/400× high power field (HPF)); mild (21–100 inflammatory cells/400× HPF); moderate (101–150 inflammatory cells/400× HPF), and marked (≥151 inflammatory cells/400× HPF). The degree of endothelialized neointima across the neck was also assessed. Histologic sections containing the proximal, mid, and distal sections were analyzed. The percentage of luminal narrowing was calculated in accordance with Kallmes *et al*.[10] The extent of stenosis was classified as follows: minimal (<20%), mild (20–35%), moderate (>35%–<50%), and marked (≥50%) (see online supplemental table 1).

Statistical analysis

Statistical analysis was performed using the statistical software SPSS version 24 (SPSS, Chicago, Illinois, USA). Continuous variables were presented as mean±SD and categorical variables as number (%). Comparisons of endothelialization, neointimal formation, or sac organization between the follow-up groups was performed using one-way analysis of variance. Statistical significance was determined at $p<0.05$ for a 95% CI.

RESULTS

Vessel and aneurysm sizes

Average aneurysm neck and sac sizes were 3.4±0.9 mm and 5.1±0.9 mm for the 1-month FU group, 3.8±0.6 mm and 4.9±1.6 mm for the 2-month FU group, and 3.5±0.5 mm and 4.7±1.9 mm for the 3-month FU group. There were no significant differences in neck or sac size among the three groups ($p=0.886$ and $p=0.591$, respectively).

Intraprocedural performance

An overview of the intraprocedural performance of the device is given in table 1.

Table 1 Overall description of intraprocedural performance in aneurysms and parent artery complexes

	DiVeRt		XCalibur
	Sidewall aneurysms n=30	Aorta n=15	n=3
Pushability	Excellent: 70% (21) Good: 7% (2) Moderate: 13% (4) Fair: 7% (2) Poor: 3% (1)	Excellent: 33% (5) Good: 13% (2) Moderate: 54% (8)	Excellent: 100% (3)
Ability of landing in target area	Excellent: 73% (22) Good: 27% (8)	Excellent: 87% (13) Moderate: 13% (2)	Excellent: 67% (2) Good: 33% (1)
Vessel wall anchoring	Excellent: 100% (30)	Excellent: 100% (15)	Excellent:100% (3)
Radiopacity	Excellent: 84% (25) Good: 13% (4) Moderate: 3% (1)	Excellent: 54% (8) Good: 20% (3) Moderate: 26% (4)	Excellent: 100% (3)
Immediate flow diversion	Excellent: 100% (30)	Excellent: 100% (15)	Excellent: 67% (2); no aneurysm: 33% (1)
No thrombogenicity	Excellent: 100% (30)	Excellent: 100% (15)	Excellent: 100% (3)
Biocompatibility	Good:100% (30)	Good:100% (15)	Good:100% (3)
Procedural safety	Excellent: 100% (30)	Excellent: 100% (15)	Excellent: 100% (3)
Foreshortening	None (100%)	None (100%)	None (100%)

In most cases the device showed excellent pushability, anchoring to the vessel wall, and excellent radiopacity. In all aneurysms, immediate flow diversion was observed.

Overall immediate postprocedural aneurysm occlusion results

At day of embolization, 66% (20/30) of all aneurysms showed OKM scale A3, 20% (6/30) OKM scale B3, 7% (2/30) OKM scale C3, and 7% (2/30) complete occlusion (OKM scale D1). All animals were available for control and end angiographies (table 2).

1-month FU group

Five rabbits were sacrificed at 1 month after DiVeRt deployment. Six aneurysms (60%) showed contrast stasis (OKM scale A3), two (20%) showed incomplete occlusion (one with OKM scale B3, one with C3), and two (20%) showed complete occlusion (OKM scale D1) immediately after device deployment. One month after treatment, all aneurysms (100%) were completely occluded (OKM scale D1), including four cases of vessel occlusion in two animals (table 2).

2-month FU group

Six aneurysms (60%) showed contrast stasis (OKM scale A3) and four (40%) showed incomplete occlusion (OKM scale B3) immediately after device deployment. At control angiographic outcome after 1 month, six aneurysms (60%) showed complete occlusion (OKM scale D1) and four (40%) OKM scale A3. At termination after 3 months, six aneurysms (60%) showed complete occlusion (OKM scale D1) and two (20%) showed incomplete occlusion (one with OKM scale B3 and one with OKM scale C3). Two aneurysms (20%) remained with OKM scale A3 unchanged at time of termination.

All parent arteries were patent at control and end angiographies, but in two aneurysms (20%) a low-grade in-stent stenosis was registered (table 2).

3-month FU group

Eight aneurysms (80%) showed contrast stasis (OKM scale A3) and two aneurysms (20%) showed incomplete occlusion (OKM scale B3) immediately after device deployment. At 3-month FU, nine aneurysms (90%) showed complete (OKM scale D1) and one (10%) incomplete occlusion (OKM scale B3). At the time of termination (6 months), 90% were OKM scale D1. The one incompletely occluded aneurysm improved regarding occlusion rate to OKM scale C3. All parent arteries were patent at the time of control and end angiographies.

Overall aneurysm occlusion rate and vessel patency

Of all the aneurysms, 93% (28/30) improved with regard to the occlusion rate. Overall, 83% (25/30) were registered with OKM scale D1. Two aneurysms (7%) improved to OKM scale C3 and one to OKM scale B3 (3%). Seven percent (2/30) remained unchanged over the control period (OKM scale A3).

Over the study period, 87% (26/30) of all animals showed parent artery patency. The remaining 13% (4/30) of aneurysms showed FD thrombosis, and aneurysm occlusion. Two of the aneurysms (7%) showed a not relevant in-stent stenosis (stenosis ranging from 20% to 35%).

Overall FU results of DiVeRt-treated aortas

In all but one aorta (7%; 1/15) patency was observed (93%; 14/15). The in-stent stenosis case was not relevant (ranging from 20% to 35%). All aortas showed side branch patency (100%).

Table 2 Postprocedural and angiographic outcome of DiVeRt-treated sidewall aneurysms: angiographic results according to the O'Kelly–Marotta (OKM) grading scale

				OKM scale				
					FU (months)			
Groups	No	Implant	Sidewall aneurysms	Post- procedural	1	3	6	Overall in-stent stenosis
1-month FU group	1	DiVeRt	Left CA	A3	D1	--	--	No
		DiVeRt	Right CA	B3	D1	--	--	No
	2	DiVeRt	Left CA	A3	D1	--	--	Yes
		DiVeRt	Right CA	A3	D1	--	--	No
	3	DiVeRt	Left CA	A3	D1	--	--	No
		DiVeRt	Right CA	A3	D1	--	--	No
	4	DiVeRt	Left CA	D1	CA occlusion	--	--	NA
		DiVeRt	Right CA	D1	CA occlusion	--	--	NA
	5	DiVeRt	Left CA	C3	CA occlusion	--	--	NA
		DiVeRt	Right CA	A3	CA occlusion	--	--	NA
	6	XCalibur	Right CA	NA	NA	--	--	No
2-month FU group	1	DiVeRt	Left CA	B3	D1	D1	--	No
		DiVeRt	Right CA	A3	D1	D1	--	No
	2	DiVeRt	Left CA	B3	D1	D1	--	No
		DiVeRt	Right CA	B3	D1	D1	--	No
	3	DiVeRt	Left CA	A3	D1	D1	--	No
		DiVeRt	Right CA	A3	A3	A3	--	Yes
	4	DiVeRt	Left CA	B3	D1	D1	--	No
		DiVeRt	Right CA	A3	A3	A3	--	No
	5	DiVeRt	Left CA	A3	A3	C3	--	No
		DiVeRt	Right CA	A3	A3	B3	--	No
	6	XCalibur	Left CA	D1	D1	D1	--	No
3-month FU group	1	DiVeRt	Left CA	B3	--	D1	D1	No
		DiVeRt	Right CA	A3	--	D1	D1	No
	2	DiVeRt	Left CA	A3	--	B3	C3	No
		DiVeRt	Right CA	A3	--	D1	D1	No
	3	DiVeRt	Left CA	A3	--	D1	D1	No
		DiVeRt	Right CA	A3	--	D1	D1	No
	4	DiVeRt	Left CA	A3	--	D1	D1	No
		DiVeRt	Right CA	C3	--	D1	D1	No
	5	DiVeRt	Left CA	A3	--	D1	D1	No
		DiVeRt	Right CA	A3	--	D1	D1	No
	6	XCalibur	Right CA	D1	--	D1	D1	No

The control animal in the 1-month FU group had no aneurysm of the carotid artery, therefore flow diversion could not be classified but patency was registered.
CA, carotid artery; FU, follow-up; No, number of aneurysms.;

Overall results using XCalibur stent-treated carotid arteries

Using the XCalibur implant, two aneurysms showed complete occlusion (OKM scale D1) and the other showed vessel patency (the animal had no aneurysm). These results remained identical at termination.

Histologic results: carotid sidewall aneurysms

Complete wall apposition of the implant was seen in all aneurysms. All aneurysms showed largely complete filling of the cavity with a loose organizing fibrous tissue matrix and adequate neck coverage with organized neointima (figure 1B).

We observed a significant increase in the percentage of endothelialization analyzed in the 3-month FU group compared with the 1-month FU group ($p<0.001$). Significantly less fibrin formation on the neck surface was detected in the 2-month and 3-month FU groups compared with the 1-month FU group ($p=0.013$). There was no statistical difference in neointima formation, which was determined to be moderate to marked ($p=0.27$). A significant decrease in inflammation ($p<0.001$) and an increase in neoangiogenesis ($p<0.001$) of the aneurysm sac was seen from the 1-month FU group to the 3-month FU group (table 3).

In four aneurysms (13%) an occlusion of the carotid artery and the aneurysm was seen on histological slides. Histologically, an increase in neointima formation in the cross-sections was detected in two carotid arteries (7%; 2/30) corresponding to the

Table 3 Histopathologic analytic parameters for semiquantitative analysis and results of histopathologic changes in all groups, including p values

Histopathologic changes	Sidewall aneurysms				Aorta			
	1-month FU group	2-month FU group	3-month FU group	P value	1-month FU group	2-month FU group	3-month FU group	P value
Platelet/fibrin thrombus	0.50±1.32	0.0±0.0	0.0±0.0	0.013*	0.0±0.00	0.0±0.00	0.0±0.00	NS
Endothelialization	3.90±0.31	3.73±0.56	3.93±0.33	<0.001*	3.67±0.30	3.7±0.48	3.9±0.15	0.038*
Neointima formation	3.98±0.14	3.97±0.30	3.96±0.29	0.27	4.0±0.00	4.0±0.00	4.0±0.00	NS
Sac organization	3.71±0.50	4.0±0.00	4.0±0.00	<0.001*	–	–	–	–
Sac inflammation	2.40±0.81	1.60±0.67	1.27±0.49	<0.001*	–	–	–	–
Sac neoangiogenesis	2.15±0.91	3.02±1.04	2.76±0.82	<0.001*	–	–	–	–

* p ≤ 0.05 is statistically significant
HPF, high power field; 400x, 40x objective +10x eyepiece, ±SEM.

DSA registered in-stent stenoses. However, due to semiquantitative analysis, these results were not statistically significant.

Histologic results: aorta

All implants were well apposed to the parent artery walls (figure 1B,C). Thrombus formation was not detected in any case. In all groups marked endothelialization was observed with a significant increase in the 3-month FU group compared with the 1-month FU group (p=0.038). In all cases the average neointimal formation was marked but equal (4.0±0.0) (table 3). The aorta detected with in-stent stenosis showed an increase in neointima formation but, due to semiquantitative analysis, this was not significant.

DISCUSSION

This study evaluated the efficacy and safety of the newly developed DiVeRt system in a rabbit aneurysm model. The study reported the performance of the DiVeRt FD and angiographic and histologic features at different periods after stent deployment.

The device was highly trackable and of appropriate radiopacity for endovascular placement using standard radiographic equipment. Immediate complete or near complete aneurysmal exclusion at the end of the implantation procedure was observed in 14% (OKM scale C3 and D1), and these results correlate with former studies which reported rates ranging from 8% to 21%.[13]

In our study over a mean FU of 3.3 months, the occlusion rate improved in 93% of aneurysms, in accordance with former studies.[14] A meta-analysis of FDs in animal models also showed improved occlusion rates after 3 months.[14]

Furthermore, the patency of small branch vessels remained excellent when covered with DiVeRt, as described in previous publications on FDs. The branch patency is likely a result of flow demand because of insufficient distal collateral supply and a favorable pressure gradient across the stent pores.[15–17]

Aneurysm occlusion

Using DiVeRt, a 90% rate of complete or near complete aneurysm occlusion (OKM scale D1 and C3) over a mean time of 3.3 months could be achieved with histologic findings of loose organizing fibrous tissue matrix within the aneurysm sac and neck coverage with endothelialized neointima within the DiVeRt. This rate of aneurysm occlusion is higher than in prior reports of aneurysm models using FDs, which showed complete or near complete occlusion rates from 61.9% to 82.6% at 3 months.[18] The rate of complete or near-complete aneurysm occlusion at 6 months was 88% in previous studies, which is comparable to this study with 90% (OKM scale C3 and D1).[16] Similar rates were documented at 6 months in an elastase-induced animal model study[19] and after 7–12 months in a sidewall aneurysm model.[10]

Histologic findings

The initial events directly after FD placement include complete denudation of endothelial cells where the FD is in contact with the parent artery as well as adherence of inflammatory cells to scattered intersections of the device at the neck.[20] Despite the reported rapid endothelialization of the parent artery, endothelialization at the aneurysm neck is usually delayed, as reported previously.[20]

The excellent occlusion rates of DiVeRt may be explained by early endothelialization in accordance with strong thrombus formation within the aneurysmal cavity. Flow disruption into the aneurysmal cavity is caused by device porosity and pore density.[21] Thrombus formation is the initial step for aneurysm occlusion due to flow disruption caused by the FD.[21] All aneurysms showed largely complete filling with a loose organizing fibrous tissue matrix and a decrease in inflammation and increase in neoangenesis over time. After intrasaccular thrombus formation, neointimal coverage of the FD surface at the neck leads to the exclusion of the aneurysm from the circulation.[20 22 23] Our histologic findings showed only little intraluminal fibrin formation but marked endothelialized neointima coverage of the aneurysm neck within the DiVeRt stent even within the first month. These results may contribute to an excellent aneurysmal occlusion rate after a mean of 3.3 months.

Adequate neoinitma formation, which is a phenomenon dependent on the design of the FD, allows the dynamic control of blood flow and regulation of inflammation.[21] In our series, stable incorporation of the DiVeRt within the arterial lumen was shown.

Poor wall apposition of the FD diminishes the positive hemodynamic effects of flow disruption.[20] Histologic analysis in our study showed adequate wall apposition in all implanted DiVeRt stents.[24] Prior studies stated that, in addition to potential hemodynamic considerations, optimal wall apposition is a key modulator of optimal aneurysm occlusion after flow diversion.[20 23] Excellent wall apposition of the DiVeRt stent contributes to good aneurysm occlusion rates because the direct stent contact with the wall is necessary to provide a scaffold for contiguous endothelial cell growth from the parent vessel, as also shown in this study.[21]

Rate of in-stent stenosis

Intimal hyperplasia and in-stent stenosis were minimal in our series. We found that 7% of the stents placed at the sidewall aneurysms and another 7% in the aorta developed in-stent stenosis. In this series the rate was lower than that reported in other FD studies, with in-stent stenosis rates as high as 39%. However, in most cases the in-stent stenosis was graded as mild, similar to the present study.[25] The in-stent stenosis grades noted in our series were not significant, as also shown in former studies.[16 25] Due to non-high-grade in-stent stenosis and dual antiplatelet treatment in our series, we think it is unlikely that in-stent stenosis rates would increase over longer time periods.

In the present study, the DiVeRt stent system showed the potential to reduce the flow within the aneurysms while providing a matrix for marked neointimal formation. The properties of this device could be the result of the specific proprietary polymer membrane that nearly spans the full length of the implant. This provides 50–60% of surface coverage instead of the 25–35% coverage of a typical neuro-flow diverter like the Pipeline Embolization Device (PED, Medtronic, Minneapolis, Minnesota, USA), the Flow Redirection Intraluminal Device (FRED, Microvention, Aliso Viejo, California, USA), SILK (Balt, Irvine, California, USA) and STREAMLINE (Stryker, Kalamazoo, MIichigan, USA). Despite the increasing use and success of FDs, there have been numerous reports of procedural complications such as FD thrombosis.[26] Full stent deployment and apposition to the vessel wall are known to be critical factors to avoid FD thrombosis and thromboembolic events.[26]

Even though all animals were treated equally with dual antiplatelet regimen, four instances of FD thrombosis occurred in our study (13%). In these cases the vessel diameters were appropriate for the chosen FD size, as well as wall apposition of the device. However, three of them showed nearly immediate aneurysm occlusion after stent placement. There are few reports of delayed FD thrombosis in the literature.[22] A meta-analysis of FDs in animal models showed only a few cases of in-stent thrombosis.[18] Another meta-analysis of 579 human aneurysms treated with FDs also showed a very small number of FD thrombosis. In this meta-analysis, only four cases of FD thrombosis were noted during the procedure and another eight during FU. In our series, the occurrence of FD thrombosis remained clinically asymptomatic, as reported in previous studies.[3 27 28] Long-term FD thrombosis may occur in an asymptomatic fashion in cases of rich blood supply from collaterals.[28] It is also reported in the literature that dual antiplatelet therapy may have a critical relationship with the occurrence of FD thrombosis.[29] Unfortunately, platelet response testing was not done.[29 30]

Limitations

In addition to the known limitations of the aneurysm sidewall model in rabbits, a further limitation was that the XCalibur stent was used as control and no direct comparison with other known FDs was undertaken.

CONCLUSION

The DiVeRt system appears to be a feasible and effective treatment of aneurysms with high rates of complete aneurysm occlusion, excellent vessel patency, and evidence of high biocompatibility. Occurrences of parent artery occlusion at follow-up did not result in clinical consequences.

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Contributors CHu, EB, JG, CHe, AO, and MA performed the measurements and analyzed the data. MKO supervised the work. CHe and BE processed the experimental data, performed the analysis, drafted the manuscript and designed the figures. CHu, EB, and MKO performed the calculations. CC, JG, and CJG supported the interpretation of the results. All authors discussed the results and commented on the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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