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Different aspects of endosaccular flow disruption in endovascular treatment of intracranial aneurysms

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Table of contents

Publications summarized in this work

1. Ozpeynirci Y, Braun M, Pala A, Schick M, Schmitz B. WEB-only treatment of ruptured and unruptured intracranial aneurysms: a retrospective analysis of 47 aneurysms. Acta Neurochir (Wien). 2019;161:1507-1513. doi: 10.1007/s00701-019-03988-0.

2. Goertz L, Liebig T, Siebert E, **Ozpeynirci Y**, Pennig L, Celik E, Schlamann M, Dorn F, Kabbasch C. Treatment of proximal posterior inferior cerebellar artery aneurysms by intrasaccular flow-disruption: A multicentre experience. AJNR Am J Neuroradiol. 2022; 43:1158-1163. doi: 10.3174/ajnr.A7566.

3. Celik E*, **Ozpeynirci Y***, Liebig T, Schlamann M, Dorn F, Lehnen N, Siebert E, Goertz L, Kabbasch C. WEB embolization versus coiling for unruptured basilar tip aneurysms: Comparison of angiographic outcomes and complication rates. Sci Rep. 2022; 12:10899. doi: 10.1038/s41598-022-15113-w.

4. Durner G, **Ozpeynirci Y**, Schmitz B, Wirtz CR, König R, Pala A. Clipping as re-treatment strategy after treatment of a cerebral aneurysm with the Woven EndoBridge embolization device: case report. J Neurosurg. 2018;23:1-4. doi: 10.3171/2017.10.JNS171528.

5. Ozpeynirci Y, Braun M, Schmitz B. CT Angiography in occlusion assessment of intracranial aneurysms treated with the WEB Device. J Neuroimaging. 2019;29:481-486. doi: 10.1111/jon.12622.

6. Rosskopf J, Braun M, Dreyhaupt J, Beer M, Schmitz BL, **Ozpeynirci Y**. Shape modification is common in Woven EndoBridge-treated intracranial aneurysms: A longitudinal quantitative analysis study. AJNR Am J Neuroradiol. 2020;41:1652-1656. doi: 10.3174/ajnr.A6669.

7. Wodarg F*, **Ozpeynirci Y***, Hensler J, Jansen O, Liebig T. Contour-assisted coiling with jailed microcatheter may result in better occlusion (CoCoJaMBO) in wide-necked intracranial aneurysms: Proof of principle and immediate angiographic results. Interv Neuroradiol. 2022 Jan. doi: 10.1177/15910199211069782.

8. Liebig T, Gal G, O Kelly C, Wodarg F, Killer-Oberpfalzer M, **Ozpeynirci Y**, Bester M, Tsogkas I, Psychogios MN, Jansen O, Fiehler J. Neqstent coil-assisted flow diverter (NQS) for the treatment of bifurcation aneurysms: the coil-assisted flow diversion safety and performance study (CAFI). J Neurointerv Surg. 2023 Jul. doi: 10.1136/jnis-2022-020056.

*= shared first authorship

Introductory summary

Intracranial aneurysms (IA) can be treated surgically or endovascularly. Although both techniques are very effective for carefully chosen patients, the balance has shifted in favor of less invasive techniques due to advances in endovascular devices and methods, which have the advantages of shorter operating times, toleration in less healthy patients, and shorter hospital stays.

Guglielmi detachable bare platinum coils, the first device of the modern era of neuroendovascular surgery, was first used in 1990. And since, endovascular coil therapy has become widely recognized as a promising treatment for IAs [9,45].

The idea of coiling is to establish dense packing in the aneurysm by delivering detachable platinum coils, which leads to the creation of a thrombus and later granulation tissue, so limiting blood flow to the aneurysm lumen (Figure 1). It does, however, have a number of drawbacks. The major downside of simple coiling is its high recurrence rate, which may be attributed to coil compaction or initial suboptimal packing density. Thus post-treatment follow-up imaging and, in some cases, retreatment [12,20,30,45,60,63,64,67] are needed. A second treatment has been reported to be about 12%, on average 27 months following the first procedure [30].

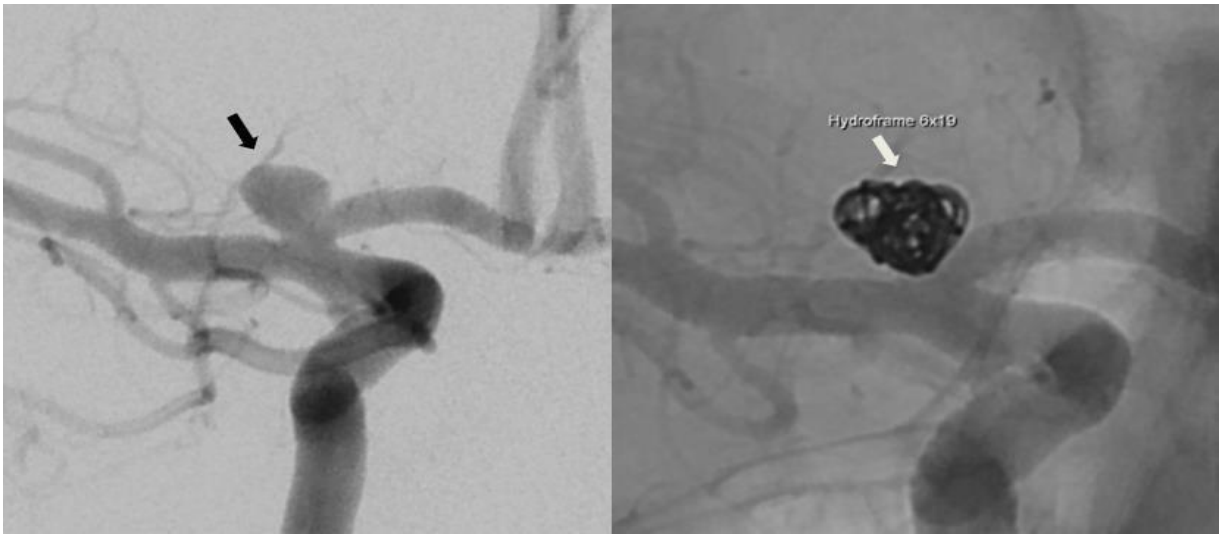

Figure 1 *Angiographic image of an internal carotid artery terminus aneurysm before (left, black arrow) and after coil occlusion (right, white arrow).*

High recurrence rates following coil embolization, particularly in large and giant aneurysms and those with a wide neck [60], have fueled a push for technical advancements in endovascular devices to enhance long-term results. Significant developments have been made, including an increasing variety of coil sizes and designs, enabling safer and more effective coiling of IAs. Procedures such as balloon remodeling [46] and stent-assisted coiling (SAC) [69] have widened the indications, allowing for the treatment of more difficult cases.

To perform the balloon remodeling technique, a compliant balloon is temporarily inflated across the aneurysm neck while a single or multiple coils are placed within the aneurysm sac. The balloon is then deflated to make sure that no coil loops move into the parent vessel before the final detachment (Figure 2). Stent-assisted coiling has been used to manage wide-necked aneurysms that coils alone or balloon remodeling cannot address. The fundamental goal of a stent implantation is to create a scaffold to protect the parent artery against coil prolaps, thus allowing coiling of wide-necked, giant, fusiform, and other complex aneurysms that are not coilable alone. Various studies have demonstrated that SAC offers a more stable aneurysm occlusion than stand-alone coiling [7,24,44,52]. The most feared aspect of SAC is the possibility of thromboembolic events. In comparison to coiling alone, several studies found

higher incidence of ischemic events following SAC [24,52]. Thus, long-term antiplatelet medication is required for stent-assisted interventions to minimize the risk of thrombus development at the metal-covered surface.

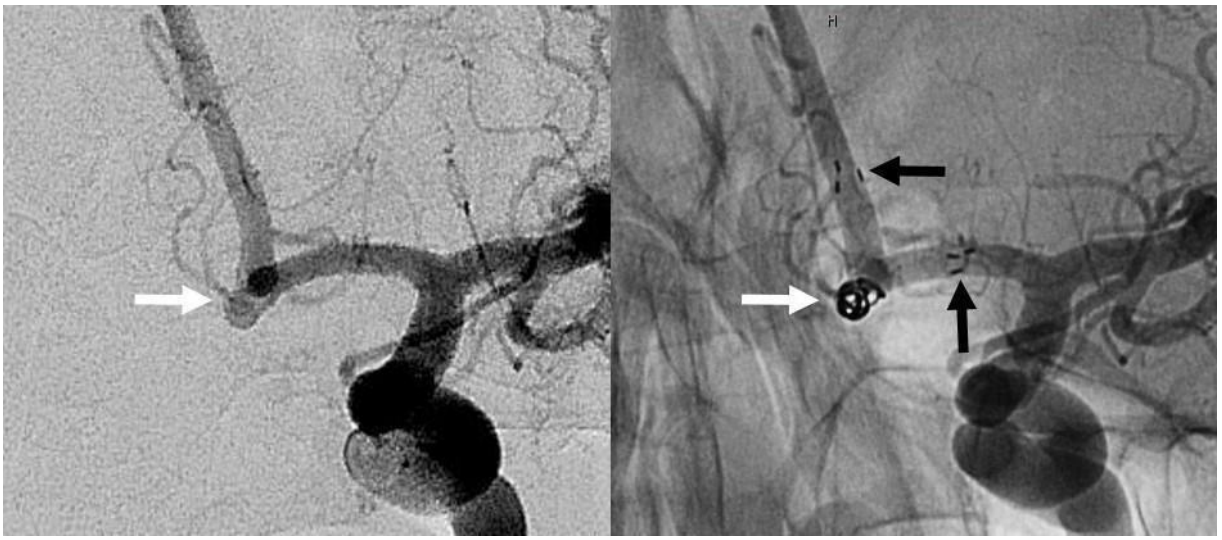

Figure 2 *DSA shows a small but wide-necked anterior communicating artery aneurysm before (left, white arrow) and after stent-assisted coil occlusion (right, white arrow). Black arrows (right) point to the proximal and distal stent markers.*

Flow diversion, which was introduced in 2009, has further altered endovascular therapies. Flow diverters are a new class of stents that are very flexible and have a less porous mesh design than the standard stents. A flow diverter is placed across the aneurysm neck along the parent artery and produces blood stasis in the aneurysm by separating blood flow between the parent artery and the aneurysmal sac, resulting in gradual thrombus development inside the aneurysm (Figure 3). The aneurysm eventually thromboses and regresses over time, while the device supports endothelialization across the neck, leading in vascular remodeling.

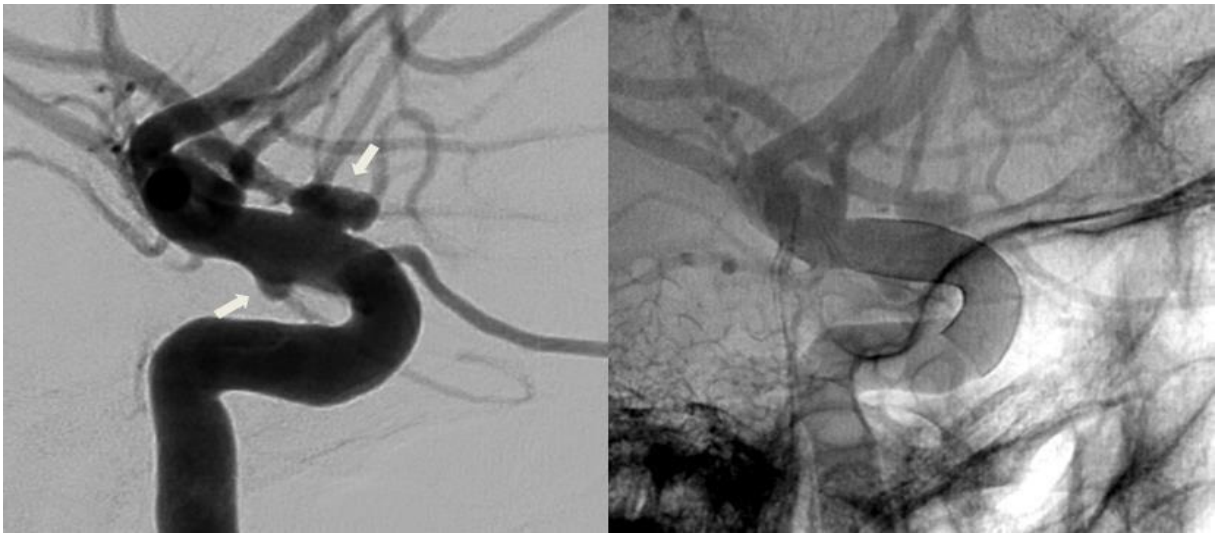

Figure 3 *Angiogram in lateral view showing two paraophthalmic internal carotid artery aneurysms before (left, white arrows) and after deployment of a flow diverter stent (right). Note the coverage of both aneurysm orifices with one stent.*

Flow diverters are meant to be utilized in anatomical scenarios where SAC becomes very complex, such as very wide-necked, giant, or fusiform aneurysms. Fiorella et al. demonstrated a 12 month complete occlusion rate of 74.9% and a primary safety event rate of 7.8% (stroke or neurologic death) in their meta-analysis that included only internal carotid artery aneurysms,

the most common location for flow diverter therapy, showing the device's efficacy and safety [26].

Endosaccular flow disruptors

Endosaccular flow disruption is a concept that evolved from flow-diverting stents in an attempt to treat wide-necked aneurysms without permanent implantation of material into the parent artery. A low-porosity mesh structure is inserted within the aneurysm sac via a dedicated microcatheter and detached electrolytically. The mesh structure then alters blood flow at the neck level and causes intra-aneurysmal thrombosis. In this regard, the process is comparable to flow diversion, with the benefit that no permanent intravascular device is used, eliminating the requirement for long-term dual antiplatelet medication.
The most well-known and widely used endosaccular flow disruptor is the WEB (Woven EndoBridge, MicroVention Terumo, Tustin, California, USA), which has been present on the European markets since 2010 (Figure 4).

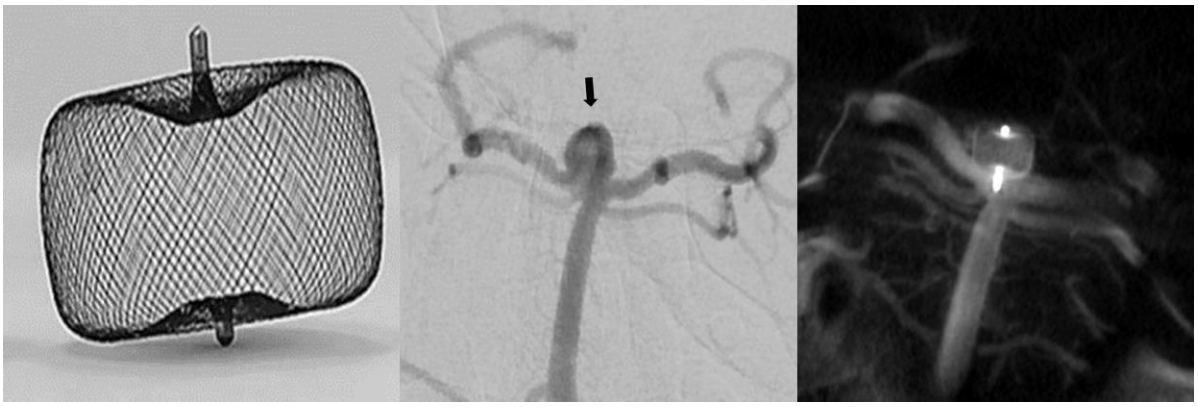

Figure 4 *Photograph of the WEB device in side view (left). Angiographic image in frontal projection demonstrating a basilar tip aneurysm (middle, black arrow). Total occlusion after WEB implantation on 3D-rendered angiographic image (right).*

The WEB is a self-expanding, totally retrievable, and electrothermally detachable device composed of nitinol braiding. It is placed into the aneurysmal sac to redirect flow away from the dome, which causes stagnation and thrombosis. The proximal surface provided by WEB offers a flat surface as opposed to the wavy surface produced by the coils at the neck level, which may provide superior support for neoendothelium. It can be used to treat incidental as well as ruptured wide-necked bifurcation aneurysms owing to unnecesstiy of antiplatelet medication following the treatment.

WEB device is often used to treat ruptured and unruptured wide-necked bifurcation aneurysm of the middle cerebral artery, anterior communicating artery or basilar artery. Numerous studies showed that the WEB device is quite safe, with periprocedural morbidity rates of about 2%, which is far lower than those previously reported for any other treatment technique of wide-necked bifurcation aneurysms, particularly SAC [3,4,5,27,37,42,47,54,66].

I conducted my first study as part of my research attempts to demonstrate the treatment outcome of ruptured and unruptured aneurysms exclusively using WEB. In a study population of 47 intracranial aneurysms, WEB achieved an acceptable thromboembolic complication rate of 12.7% and a hemorrhagic complication rate of 4.2% while providing stable aneurysm occlusion in 93.7% of aneurysms without the need for additional intervention over an average follow-up duration of nine months [50].

We assessed the treatment outcome of aneurysms using the WEB device in individual locations (proximal posterior inferior cerebellar artery (PICA) and basilar artery tip) in the two following multi-center trials. In the first study, we discovered that after a median follow-up of 6

months, none of the 15 patients who had PICA aneurysms treated with WEB required retreatment. We determined that a WEB treatment of aneurysms at that location is effective and safe without treatment-related permanent morbidity in our series [28].

We evaluated unruptured aneurysms at the basilar artery tip in the second multi-center trial and compared the angiographic results and complication rates of WEB embolization and coiling. There were forty WEB patients and thirty-five coiling patients in the study. Despite similar complication rates and mid-term angiographic findings amongst the groups, WEB was associated with a shorter intervention time and less need of stent support [16].

We presented the first case in the literature of a recurrent aneurysm after initial occlusion with a WEB device that was treated by neurosurgical clipping. In contrast to the coils, its softness and compressibility allowed for simpler clip placement without the necessity for WEB removal. Furthermore, because of the WEB device's transparency, indocyanine green (ICG) angiography data were easily interpreted, offering a great assessment of clip position in our case. Clipping proved to be a successful therapeutic option for rare aneurysm recurrences following WEB therapy [23].

In another trial, we concentrated on non-invasive imaging follow-up of WEB patients. The role of CT Angiography (CTA) in occlusion evaluation of cerebral aneurysms treated with the WEB device was investigated. Using the κ statistic to evaluate interobserver and intermodality agreement for CTA and digital subtraction angiography (DSA) (the gold standard), we were able to demonstrate good intermodality agreement for aneurysm remnant identification. For identifying an aneurysm remnant, CTA showed a sensitivity of 50%, a specificity of 100%, a positive prediction value of 100%, and a negative prediction value of 93.33%. We concluded that CTA is a valid and reproducible approach for evaluating an aneurysm's occlusion status, and it has the potential to be used in the non-invasive follow-up of aneurysms treated with WEB as an alternative or adjacent to MRA [51].

The WEB may undergo a shape change or a compression phenomenon throughout the follow-up, which may be associated with a worsening of aneurysm occlusion or re-opening [14,32]. We retrospectively performed a quantitative examination of the evolution of the WEB's shape over time in connection to imaging outcome in 32 aneurysms during the course of a median follow-up period of 11.4 months. Shape change was a prevalent occurrence (90.6%) in cerebral aneurysms treated with WEB, with a median height decrease of 19.2% after a year. Contrary to what has been reported in the literature, the aneurysm occlusion quality in our research cohort was not affected by this change in structure [61].

The Contour Neurovascular System and Neqstent Coil Assisted Flow Diverter (Cerus Endovascular, Fremont, CA, USA), which were recently brought to the market as novel endosaccular flow disruptors, are currently undergoing clinical evaluation. The Contour Neurovascular System has a central, proximal platinum marker and is built from a double layer of 72 nitinol wires. The device has a disc-like form while unconstrained, and when it is inserted into the aneurysm sac, it takes on a cup-like shape, covering the aneurysm's neck and serving as a flow disruptor (Figure 5). The Contour device proved to be safe and effective in a prospective, multi-center, single-arm study for treatment of nonruptured bifurcation aneurysms (n=32 aneurysms) [41] and in a recent single-center series of 60 unruptured intracranial aneurysms [8]. Contour differs from WEB in that it is completely positioned at the aneurysm neck rather than in the sac (Figure 6).

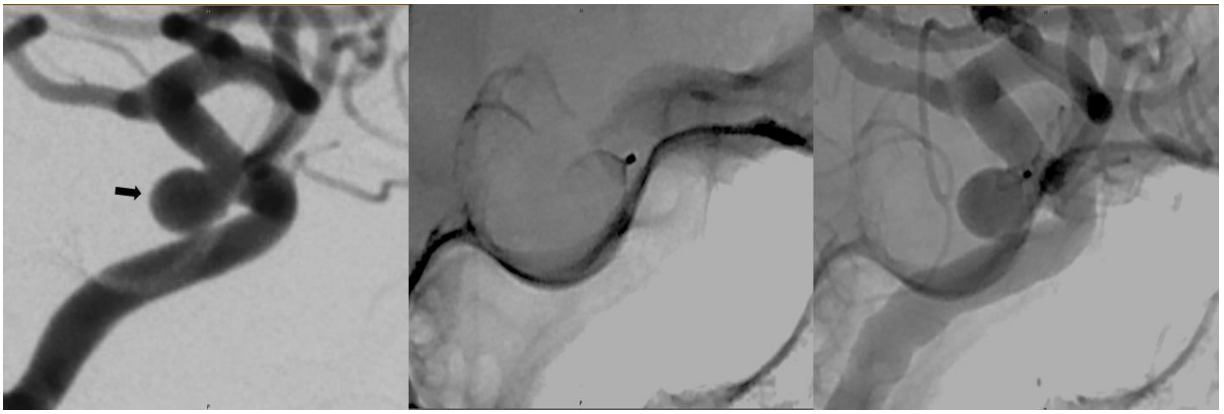

Figure 5 *Endovascular occlusion of a paraophthalmic internal carotid artery aneurysm with a Contour device. Initial angiogram in lateral view before treatment (left, black arrow). Proper device opening on X-ray image in the middle. Nonsubtracted image demonstrating adequate positioning of the device at the neck level (right).*

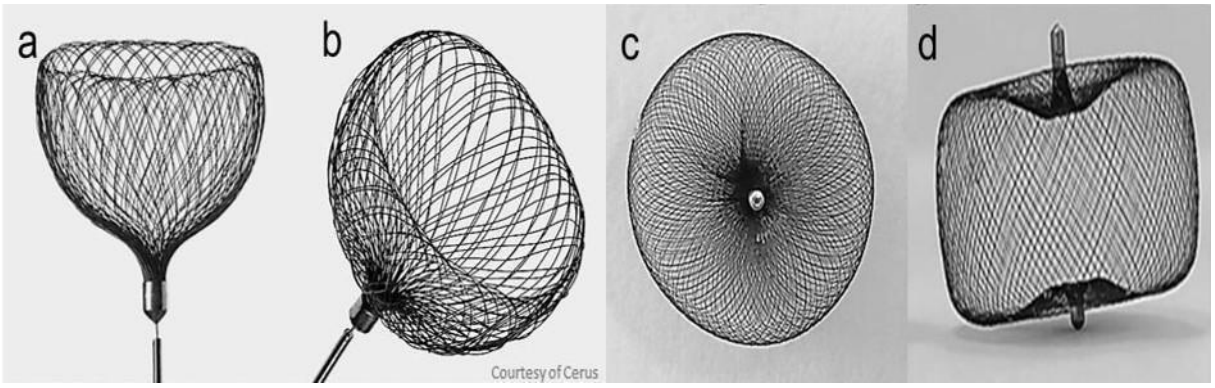

Figure 6 *Contour device in side (a) and oblique view (b). WEB device in top (c) and side (d) view. Adapted from* Effect of endosaccular flow disruption devices on procedural radiation dose and fluoroscopy time in endovascular treatment of intracranial aneurysms*. (Özpeynirci Y, 2022, p. 11, Dissertation, LMU München)*

We reported our experience with use of coils in conjunction with the Contour device to treat wide-necked aneurysms. Despite the fact that Contour is designed to be used as a single device, it is theoretically possible to coil the sac via a separate microcatheter. It would promote aneurysm occlusion while stabilizing and preventing the Contour from migrating into the aneurysm. We reported 8 cases treated with this approach in our multi-center investigation. High initial complete occlusion rates (62.5%) could be attained in this group consisting mostly of larger-sized aneurysms. No new neurological problems associated with the therapy appeared. Thus, it proved to be safe, feasible, and effective in short-term [74].

In 2020, the conformité européenne (CE) mark was approved for the Neqstent Coil Assisted Flow Diverter (NQS), a woven neck bridging device with flow-diverting qualities that enables catheterization of the aneurysm for additional coiling.

With 48 drawn-filled tube wires as opposed to 72, it shares the same morphology as the Contour. It covers the neck after being deployed through a microcatheter and conforms to the bottom portion of the aneurysm. Like with the Contour, sizing is determined solely by the aneurysm neck width. One of the advantages over the Contour is the ability to cross the device with the microcatheter and insert coils into the aneurysm by crossing instead of having to jail it. This permits reentry into the aneurysm in case the microcatheter position is lost and enables a higher coil packing density.

Our last publication, the CAFI trial, presented a prospective, single-arm, multi-center investigation on the efficacy and safety of using platinum coils in conjunction with the NQS to treat unruptured wide-necked intracranial aneurysms. Four out of the thirty-eight patients treated with this approach (10.5%) experienced device-related adverse events, three of which were thromboembolic and one hemorrhagic. Immediate post-treatment adequate occlusion was observed in 9/36 (25%) and proceeded to 28/36 (77.8%) at 6 months. This method seemed useful for treating intracranial wide-necked bifurcation aneurysms; nevertheless, larger series are needed to confirm its safety [39].

The chapters that follow go into further depth on the results of the studies.

1- Treatment of intracranial aneurysms with the WEB device only
(**Özpeynirci et al.** *Acta Neurochirurgica 2019*)

Although the feasibility, safety, and effectiveness profiles of WEB were shown in multiple clinical trials, it may be challenging to accurately portray the true potential of this technology because the majority of published trials also included aneurysms treated with additional devices like coils or stents [4,5,27,42,47,54,66,67]. This retrospective study's objective was to assess the efficacy of WEB-only therapy for ruptured and unruptured aneurysms in a single center.

All patients who had endovascular therapy for the treatment of intracranial aneurysms at our institution between April 2013 and July 2018 using just the WEB device were identified by a retrospective search of our database. Aneurysms treated with additional coils or stents were not included. Patient and aneurysm characteristics and treatment specifics, as well as occlusion status at follow-up were all recorded for each patient and aneurysm.

On follow-up, aneurysm occlusion was evaluated using by the Raymond-Roy occlusion classification (RROC): complete occlusion (RROC I), neck remnant (RROC II), and aneurysm remnant (RROC III) (Figure 7). Adequate occlusion was defined as either complete occlusion or neck remnant.

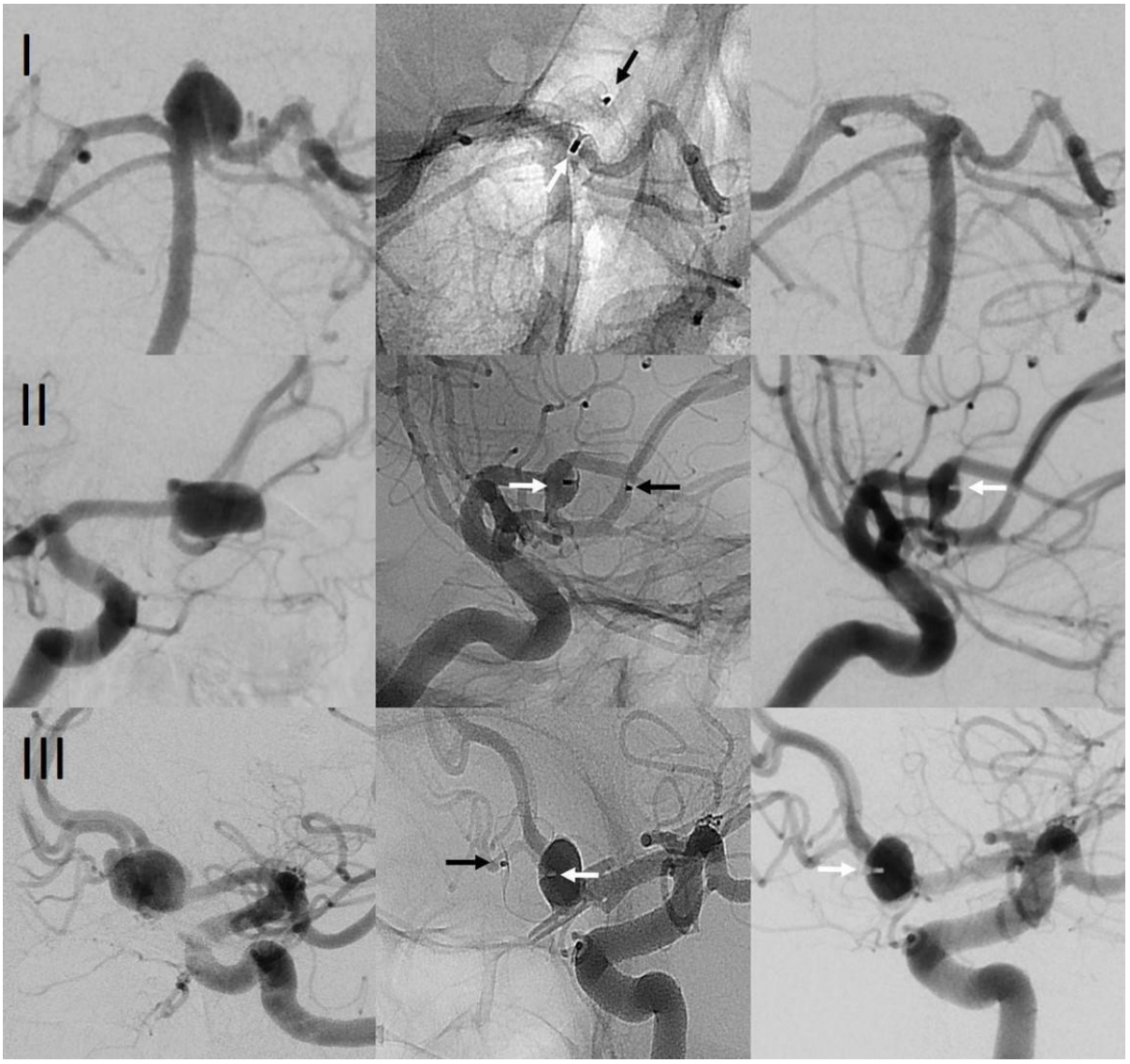

Figure 7 *Raymond-Roy occlusion classification (RROC): complete occlusion (RROC I) (upper row), neck remnant (RROC II) (middle row), and aneurysm remnant (RROC III) (lower row). Middle and right columns demonstrate follow-up. Note the shape change of the WEB device on follow-up. White and black arrows point to proximal and distal WEB markers, respectively (middle column). On the right column, white arrows show neck (II) and aneurysm remnant (III).*

The study comprised 47 aneurysms in 45 patients (33 female; 73.3%), aged 60 years (range, 36-80), treated solely with WEB device, and had at least a 3-month follow-up imaging.Twelve (25.5%) of the 47 aneurysms were ruptured. Thirty-one aneurysms (65.9%) were categorized as wide-necked aneurysms. The aneurysms measured averagely 6.3 mm (range 4-12.3 mm).

We found that the adequate occlusion rate after a median follow-up of 9 months was better (91.4%) than reported in the prospective studies and meta-analyses (79-85%). Our study's retreatment rate (5.6-8%) was in line with the literature [4,5,27,42,47,54,66,67]. Only three aneurysms (6.3%) underwent retreatment.

Our series' thromboembolic incident rate (6/47, 12.7%) was similar with previously published data (8-14.4%) [4,5,27,42,47,54,66,67]. The majority happened during the procedure or early post-procedural period prior to hospital discharge. All but one patient departed the clinic without having any residual effects. Upon discharge he had a slight one-sided leg paresis due to an anterior cerebral artery infarction.

Two patients (4.2%) had hemorrhagic problems, which was consistent with the meta-analyses'

reported range of 1.2 to 6% [4,5,27,42,47,54,66,67]. Both were reruptures of acutely ruptured anterior communicating artery aneurysms. In the first case, the rerupture happened during navigation of the microcatheter into the aneurysm and in the second case, it occured during WEB deployment. Both times, bleeding could be quickly controlled, allowing patients to recover completely.

Only one patient in our cohort with a wide-necked, unruptured middle cerebral artery bifurcation aneurysm required the placement of a stent because of an acute thrombotic occlusion of a branch caused by WEB prolapse. The employment of adjunctive devices in the literature is largely operator-dependent, with up to 15.3% documented [40]. Nonetheless, newer studies with less stringent inclusion criteria for the size and location of aneurysms revealed very little to no usage of adjunctive devices [4,27,72,73].

In our experience, the true benefit of WEB is apparent in ruptured wide-necked bifurcation aneurysms that would otherwise be treated with a more complex approach, such as stent-assisted coiling, involving the administration of antiplatelet medications. The recent advent of smaller-sized devices and low-profile delivery systems broadened the indications and allowed for stable catheterization of more distal and smaller aneurysms even in situations of severe vasospasm.

Depending on the degree of device prolaps into the parent artery or the aneurysm's neck size, double or single antiplatelet therapy may be continued in WEB cases for a shorter amount of time than is necessary for stent-assisted coiling.

The retrospective nature of this study, self-reporting of angiographic data, and small number of patients are all limitations. The study's strength is that it included a homogeneous sample of aneurysms with WEB-only therapy.

WEB-only treatment, we conclude, allows adequate occlusion of ruptured and unruptured intracranial aneurysms with high technical success and consistent outcomes at short- and mid-term follow-up without the need for long-term dual antiplatelet medication. The advantage is most noticeable in wide-necked aneurysms, which would normally be treated primarily with stent-assisted coiling.

2- Treatment of proximal posterior inferior cerebellar artery aneurysms with the WEB device
(Goertz L…**Özpeynirci Y**…Kabbasch C. *American Journal of Neuroradiology 2022*)

In this study, we reported our multi-center experience with the WEB in the treatment of wide-necked proximal PICA aneurysms. Aneurysms of the PICA are uncommon, accounting for 0.5%-3.0% of all cerebral aneurysms. The majority of PICA aneurysms develop in the proximal (anteromedullary) PICA segment, close to the PICA-vertebral artery junction [34]. PICA aneurysms can be treated surgically or endovascularly, however endovascular embolization is now preferred, since surgical therapy is linked with a high risk of neurologic complications due to the aneurysm's close proximity to the brainstem and lower cranial nerves [9].

Chalouhi et al. [18] presented the largest series on endovascular treatment of PICA aneurysms to date including 76 patients treated with conventional coiling, stent-assisted coiling, balloon-assisted coiling or parent artery closure. The rate of technical success was 96%. Complications were documented in 12.7% of the cases, and permanent morbidity was reported in 2.8%. The parent artery might be maintained in 90% of proximal PICA aneurysms.
Conventional coiling is usually possible for small-necked aneurysms, however recurrence rates have been reported to be greater than 20% [18]. Additionally, PICA aneurysms may have a large neck, necessitating stent- or balloon-assisted coiling or flow diversion.
Even if stent implantation is achievable, the PICA's small caliber increases the risk of acute thrombotic stent occlusion. The idea of endosaccular flow disruption has not yet been thoroughly investigated in the context of PICA aneurysms. The current case series describes our preliminary multi-center experience with the WEB in treating PICA aneurysms.

Between 2011 and 2021, all patients treated with the WEB for a PICA aneurysm at three neurovascular institutes (Universitätsklinikum München, Köln, and Bonn) were evaluated retrospectively and included on an intention-to-treat basis. During the study period, 16 patients with PICA aneurysms were treated at the three hospitals, with a median patient age of 60.5 years (range, 48-78 years), and all patients were female. There were seven ruptured aneurysms (43.8%). The median size of the aneurysm was 3.9 mm (range: 2.2-12.0 mm), while the median neck width was 3.4 mm (range, 1.7-7.4 mm).

Treatment only with WEB implantation was possible in 13 of 16 aneurysms (81%). WEB embolization failed in one case due to WEB protrusion, and further stent insertion was required in two other cases to enhance WEB placement.

Three peri-procedural complications (18.8%) occurred without significant long-term neurological sequelae (two thromboembolic and one hemorrhagic; rerupture of a ruptured aneurysm).

In the final 14 patients who received WEB treatment, all had complete aneurysm occlusion or just neck remnants at mid-term angiographic follow-up (median 6 months), which compares well to the 21% recurrence rate reported by Chalouhi et al. [18] for coiling. In all patients, the PICA remained patent both during the intervention and the follow-up.

The current study's limitations include a small study population and a retrospective methodology. Finally, the long-term angiographic results were missing.
In conclusion, the findings suggest that the WEB is appropriate for proximal PICA aneurysms, providing satisfactory angiographic outcomes as well as acceptable safety.

3- WEB-treatment vs coiling for unruptured aneurysms located at the tip of basilar artery
(Celik E, **Özpeynirci Y**… *Scientific Reports 2022*)

Approximately 8% of all intracranial aneurysms are basilar artery tip aneurysms (BTA) [10,13]. Endovascular therapy has replaced microsurgical clipping as the preferred method of treating BTA because of their close proximity to the brainstem and the narrow surgical corridor. Due to the frequent wide-necked anatomy of BTAs, conventional coiling is oftentimes impractical and may be linked to recanalization rates of up to 40% [17,31,45,65]. Due to the complex anatomy of the basilar artery tip, e.g. four vessels arising from it, stenting might be technically challenging. SAC has demonstrated greater aneurysm obliteration rates than stand-alone coiling [56]. However, higher incidence of complications, particularly thromboembolic events, and the requirement for long-term antiplatelet medication are drawbacks of stent implantation [6,29,57].

The WEB device, in contrast, is an excellent substitute since it is fully implanted into the aneurysm sac while leaving the parent artery intact. With proper size selection, the WEB could protect the vessels originating from the aneurysm base.

This study's goal was to evaluate the procedural risks, clinical outcomes, and mid-term angiographic outcomes of the WEB with those of coiling with or without stent support for the treatment of unruptured BTAs. Only aneurysms that could be treated with either method were included.

Retrospective identification was done for all unruptured BTAs that were treated with WEB or coiling, with or without stent or balloon support. In the first half of the research period, coiling was primarily used, and in the second half, WEB embolization was primarily used. Records of patient and aneurysm characteristics, treatment details, and occlusion status at follow-up were reviewed. The Raymond-Roy occlusion classification (RROC), as described above, was used to assess aneurysm occlusion at follow-up (Figure 7).

The final study population included 40 patients who received WEB treatment and 35 individuals

who received coiling. Only the aneurysmal neck width was significantly different in the WEB group (mean 4.7 mm) as compared to the coiling group (mean 3.9 mm) among the baseline patient and aneurysm parameters (age, sex, aneurysm dome with, height, neck, and dome width-to-neck width ratio). The remaining baseline traits showed no significant difference.

WEB and coiling were both related with comparable complication rates, morbidity, and angiographic outcomes regarding the treatment of unruptured BTA aneurysms. In contrast to the WEB, coiling required stent support far more frequently (3% and 71%, respectively). Furthermore, procedure time, radiation exposure, and contrast dye administration were reduced in the WEB group, although not statistically significantly different, most probably owing to the use of stents in the coiling group.

The non-randomized retrospective design, the small sample number, and the self-assessment of the aneurysm occlusion status are the main drawbacks of this study. Additionally, not all patients had long-term follow-up, which might affect long-term clinical and angiographic data. Finally, the neurointerventionalist's evaluation was used to decide the treatment regimen. As a result, we cannot rule out any potential prejudice towards a specific approach.

We believe that aneurysms with a diameter of less than 11 mm (the biggest WEB size currently available on the market), a wide-neck form, and a saccular shape are suitable for the WEB. Larger and more anatomically complicated aneurysms should be treated using SAC, flow-diversion, clipping, or a combination of these modalities rather than the WEB.

4- Clipping of a recurrent aneurysm previously treated with WEB
(Durner G…**Özpeynirci Y**…Pala A. *Journal of Neurosurgery 2018*)

We reported the first case of surgical clipping following prior embolization with the WEB device. A 49-year-old woman with two incidental aneurysms, one at the anterior communicating artery (Acom) and the other at the basilar bifurcation, were treated with WEB device. DSA revealed a recurrence of the Acom aneurysm at the initial follow-up, 6 months after the intervention, necessitating retreatment. There was no sign of recanalization of the basilar aneurysm. A right supraorbital approach was used for the surgery (Figure 8). A 7-mm straight clip was used to close the aneurysm (Lasic Aneurysm Clip System, Peter Lasic GmbH). ICGA was done intraoperatively, and the clip had to be adjusted twice to ensure full aneurysm closure. ICGA verified parent vessel patency (Figure 9) as well as complete aneurysm occlusion. The patient's postoperative course was uncomplicated, with no neurological impairments seen. DSA confirmed complete aneurysm occlusion. The patient was released home six days following surgery. There were no late problems noted throughout the follow-up period.

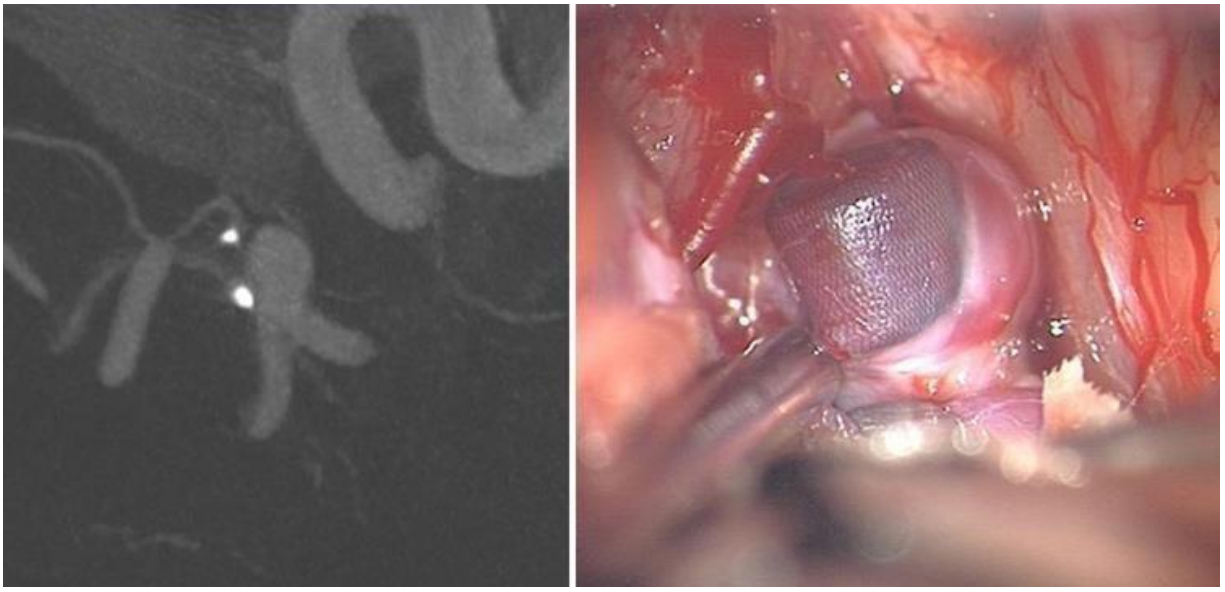

Figure 8 *CT angiography image with maximum intensity projection reconstruction (left) and intraoperative photograph (right) of a recurrent anterior communicating artery aneurysm.*

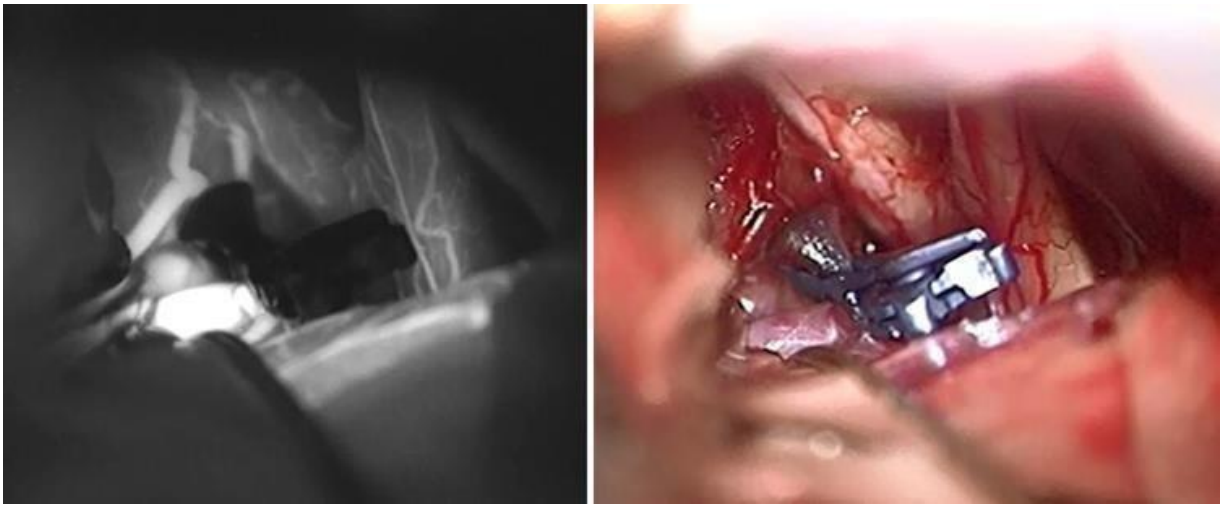

Figure 9 *ICG angiogram (left) and intraoperative photograph (right) of the anterior communicating artery aneurysm after re-treatment using a 7-mm clip, confirming aneurysm occlusion.*
Reprinted from Clipping of a recurrent aneurysm previously treated with WEB*, Durner G et al., Journal of Neurosurgery 2018, p. 2, 3.*

Clipping previously coiled aneurysms has been a common procedure in recent years, resulting in high occlusion rates and favorable clinical outcomes [21]. In virtually all cases, surgical clipping provides a permanent treatment, and if aneurysm occlusion is confirmed by DSA, recurrence is quite unlikely [58]. As innovative endovascular devices have been developing, re-treatment methods for recurrent aneurysms after their application need to be reevaluated.

Clipping of a previously WEB-treated aneurysm varies in multiple ways from clipping of a previously coiled aneurysm:

1- In some cases, surgical coil removal may be required because of the coil protrusion into aneurysm neck or parental arteries, which prevents satisfactory clipping. However, coil extraction appears to increase the chance of stroke, which might cause a serious neurological disability [21]. Given the characteristics of this device, such as being a single implant in the aneurysm sac and the compression phenomenon occuring over time leaving the neck region mostly free of material in case of a recurrence, the need for device removal might be low.
2- Clip placement was simple due to WEB's compressibility, eliminating the need to remove the WEB device.
3- Additionally, in our situation, intraoperative ICGA was quite helpful. Since coils can mask aneurysm filling and make it more difficult to detect intraluminal blood flow, the assessment of intraluminal patency and aneurysm occlusion may be more challenging. The WEB device's transparency made it possible to clearly comprehend the results of an ICG angiography, which allowed for a great evaluation of the therapy in our situation following clip positioning.

In conclusion, clipping might be a good alternative for re-treatment of recurrent aneurysms previously treated with WEB.

5- The role of CTA in occlusion assessment of aneurysms treated with WEB
(**Özpeynirci et al.** *Journal of Neuroimaging 2019*)

Although digital subtraction angiography (DSA) has been acknowledged as the gold standard in the follow-up of aneurysms treated with the WEB device, there are unresolved problems in the literature about the choice of noninvasive imaging modalities in the mid- and long-term follow-up. Time-of-flight (TOF) and contrast-enhanced (CE) magnetic resonance angiography (MRA) have been the subject of published research with encouraging outcomes, but the capabilities of computed tomography angiography (CTA) have not yet been in-depthly examined [43,68,70] To the best of our knowledge, there has only been one study that

evaluated the function of CTA in WEB-treated patients [59].

In this article, we compared the occlusion status of aneurysms treated with the WEB device using CTA to that of DSA and showed the degree of repeatability of CTA results.

To assess interobserver and intermodality agreement for each approach, we employed the κ statistic. We determined the sensitivity, specificity, negative predictive value, and positive predictive value for CTA from a 2x2 contingency table using DSA as the gold standard to identify aneurysm remnant.

Only patients who were treated only with the WEB device and had a CTA and a DSA done during the same hospital stay were included in the study. Two interventional neuroradiologists independently reviewed each pair of scans (DSA or CTA) in a random sequence at least one week apart from one another. Then, with the guidance of a more experienced neuroradiologist, agreement was reached between two interpreters in cases of conflict. The follow-up results were withhold from the neuroradiologists.

The Raymond-Roy occlusion classification (RROC), as described above (Figure 7), and a binomial scale were used to assess aneurysm occlusion at follow-up. The binomial scale was defined as either adequate occlusion (complete occlusion and neck remnant) or aneurysm remnant.

The study comprised 16 aneurysms that met the criteria. CTA and DSA images from the intervention had to be compared in 11 (68.75%) patients. The median duration between the DSA and the CTA was three days (range 0-18 days).

Two observers were in agreement in 15 of 16 CTAs (93.75%) and 14 of 16 DSAs (87.5%) using the binomial scale, indicating strong interobserver agreement for CTA and moderate interobserver agreement for DSA.

CTA and DSA were in agreement in 15 of 16 aneurysms (93.75%) following a consensus reading using the binomial scale, indicating high intermodality agreement for aneurysm remnant identification. There was disagreement on one aneurysm remnant on DSA that CTA failed to detect. The prevalence of aneurysm remnant was 12.5% in the study population.

CTA had a sensitivity of 50%, a specificity of 100%, a positive prediction value of 100%, and a negative prediction value of 93.33% for detecting an aneurysm remnant.

DSA continues to be the standard imaging method for monitoring aneurysms that have been treated with the WEB device. MRA is the most researched noninvasive imaging modality in the follow-up of these aneurysms [43,68,70]. According to the published studies, the intermodality agreement between MRA and DSA was comparable to that between CTA and DSA in our series [43,68].

However, MRA has two challenges. The neck area of the aneurysm and the parent artery cannot be evaluated very well due to susceptibility artifacts caused by disturbances of the homogeneity of the magnetic field within and around the implant. Additionally, electrically conductive nature of the WEB causes a Faraday cage effect, which impairs vision of the inside of the WEB [48,68]. According to our opinion, CTA is superior than MRA, particularly in the identification of persistent contrast enhancement inside the WEB, a distinct phenomena associated with this device in short- or mid-term follow-up. With 100% agreement with DSA, CTA was able to identify such contrast enhancements in 5 cases (Figure 10).

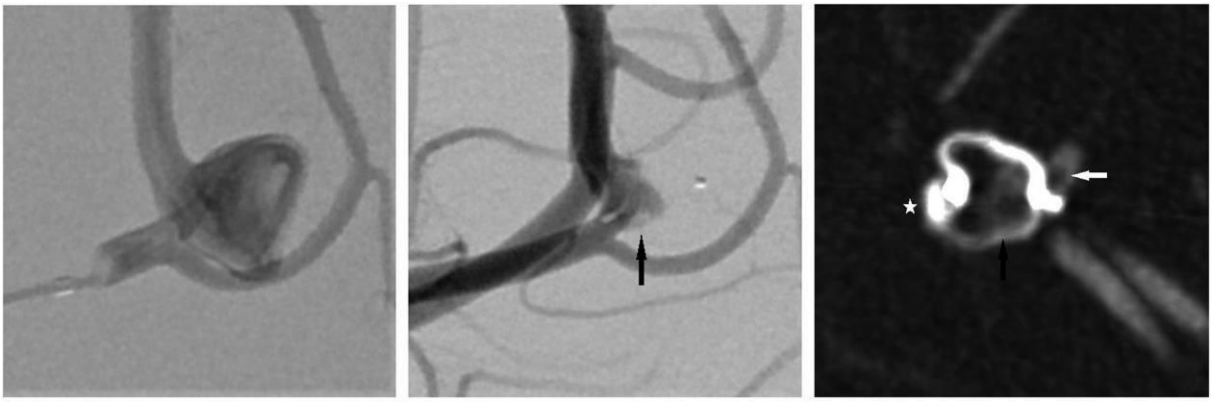

Figure 10 *Ruptured left anterior cerebral artery bifurcation aneurysm (A). Slightly bulging of the WEB into the parent artery following detachment (black arrow on B). CTA demonstrates a thrombus in the pericallosal artery (white arrow on C) and persistent contrast enhancement inside the WEB (black arrow) 18 days after treatment. Note the aneurysm wall calcification at the dome (white star on C). Reprinted from* CT Angiography in Occlusion Assessment of Intracranial Aneurysms Treated with the WEB Device, *Ozpeynirci Y et al., J Neuroimaging 2019, p. 484.*

The percentage of aneurysms followed up by CTA is quite low in large WEB case series [54,55,72,73]. Only one study performed by Raoult et al. compared directly DSA and CTA in follow-up of aneurysms treated with a WEB device. Similar findings were made when they assessed the diagnostic performance of CTA at a 1-year follow-up of aneurysms treated with the WEB [59].

Finally, we think that CTA can be used as an alternative or adjunct to MRA for the noninvasive follow-up of aneurysms treated with the WEB device since it is a reliable and reproducible method for evaluating the aneurysm occlusion status. In particular, it was able to clearly illustrate the subgroup of aneurysms with persistent contrast enhancement inside the WEB.

6- Shape modification of WEB device on follow-up
(Rosskopf J…**Özpeynirci Y**. *American Journal of Neuroradiology 2020*)

The alteration of the WEB shape (i.e., a reduction in height or a reduction in the distance between the proximal and distal markers of the WEB device) is a phenomena that is frequently observed during follow-up and may be linked to a worsening of aneurysm occlusion status [19,62,67]. Thoughts on the underlying mechanisms range from clot retraction to high artery inflow, and investigations into these mechanisms are rare [14,32,35,53]. Quantitative assessment of WEB shape alteration might be useful for analyzing anatomic findings over time. It's important to note that, up until this point, only one previous DSA-based study has presented descriptive findings from a quantitative WEB shape-modification evaluation without conducting association analysis [35].

The goal of the current study was to measure the WEB device's height decrease during the course of mid- and long-term follow-up. Based on the results of DSA studies [11,35], we predicted that the height loss detected on subsequent CT scans using a semi-automated method would be frequent in WEB-treated aneurysms and would correspond with time. Furthermore, it was not anticipated that WEB form alteration would have any effect on the aneurysm occlusion quality. Finally, association studies with anatomic and clinical factors, such as device size, aneurysm rupture status, aneurysm location, and re-intervention rates, were carried out.

From our institutional data base, all patients who received endovascular therapy using a WEB device between April 2013 and April 2020 were gathered. The inclusion criteria were cranial CT at baseline (the day of the intervention) and a follow-up CT at least 1 month later.

The evaluation of the imaging data was done independently and in random order. Together, the 3-grade classification and the distinction between adequate and inadequate occlusion

served to identify the quality of aneurysm occlusion (Figure 7). As described above, complete occlusion or neck remnant were both referred to as adequate occlusion.

Reduction of the device height was utilized as a marker for form alteration. Reduction in height was measured on cranial CT scans with a slice thickness of 0.54 mm using ImageJ 1.52a software in a semi-automatic multistage method (National Institutes of Health) (Figure 11).

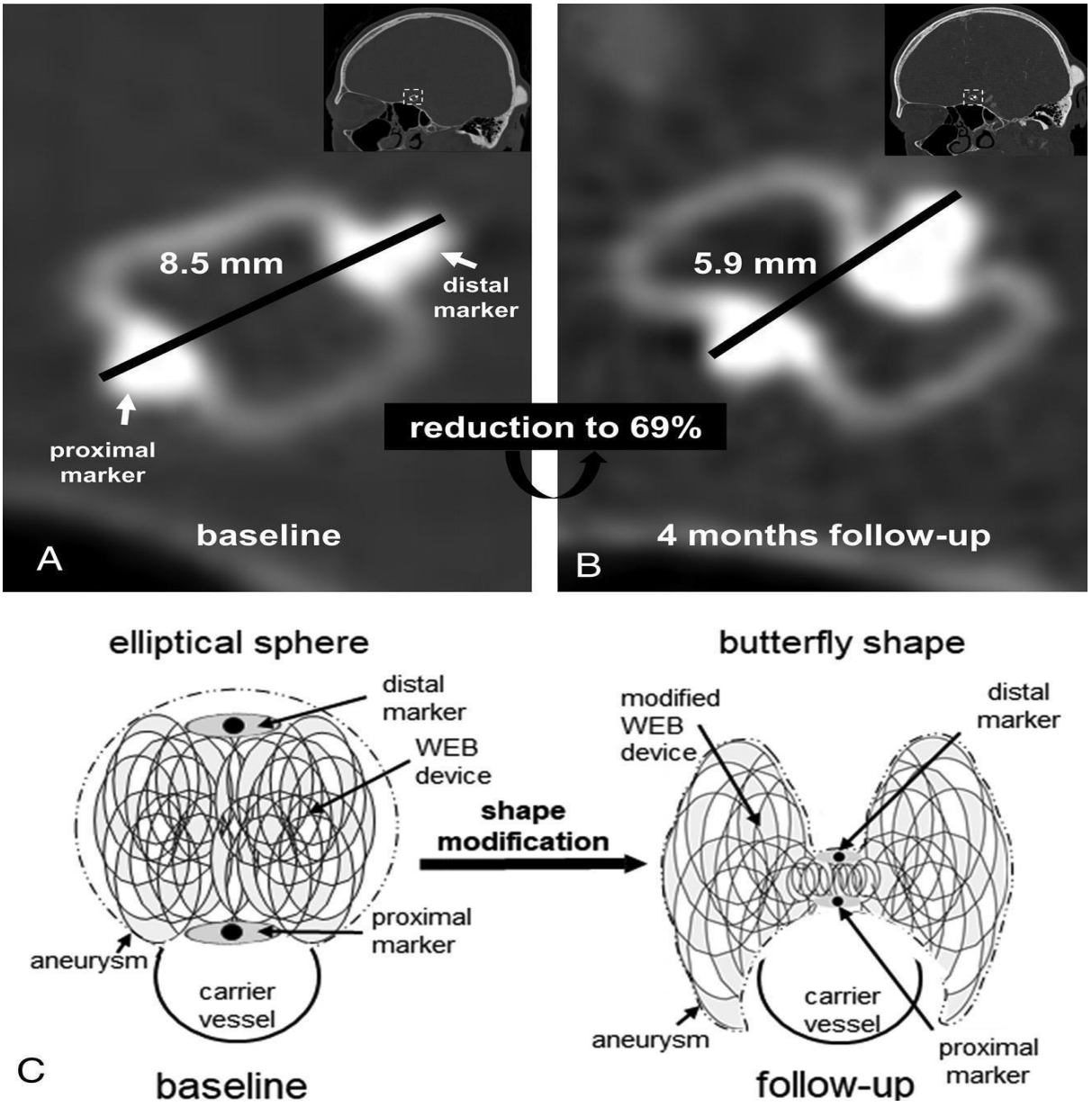

Figure 11 *Anterior communicating artery aneurysm treated with a 7 x 4 mm WEB device. CT at the postoperative day 0 (A) and 4 months later (B). The distance (black line) between the proximal and the distal marker decreases from 8.5 to 5.9 mm, yielding a reduction to 69%. Schematic illustration (C) of WEB shape modification from an elliptical sphere to a "butterfly figure" on follow-up. Reprinted from* Shape Modification is Common in Woven EndoBridge-Treated Intracranial Aneurysms: A Longitudinal Quantitative Analysis Study*, Rosskopf J et al., AJNR Am J Neuroradiol. 2020, p. 1654.*

Analytical and graphical time course evaluation of WEB shape alteration was carried out. The median yearly decrease was calculated as a result of this.

During the follow-up of 32 WEB-treated aneurysms, we statistically studied shape alteration of the WEB device and assessed its correlation with anatomic outcomes.

The inclusion criteria of baseline CT and follow-up CT at least more than one month later were met by thirty patients with 32 aneurysms that had had WEB treatment (two patients had two

aneurysms).

WEB devices were ranging in size from 3.5 X 2 mm to 11 X 9 mm. The CT follow-up had a median duration of 11.4 months. Long-term data with a follow-up period longer than 18 months were available in 31.3% of cases.

WEB-treated aneurysms frequently (90.6%) underwent shape alteration on CT images. The decline in height over time was statistically significant. Shape change was not significantly correlated with aneurysm occlusion quality, device size, aneurysm rupture status, aneurysm location, or re-intervention rate. With a median decrease of 19.2% each year, the visual and analytical assessment of time courses indicated diverse patterns of shape alteration. A larger drop in WEB height was associated with a longer period after the intervention, with an average of 0.017% decrease per day. The change in height over time was strongly correlated with the number of days since the intervention.

As an unique component of the present investigation, the shortening of the distance between the proximal and distal marker of the WEB device as a proxy for shape modification was analyzed quantitatively on CT scans using a semi-automated approach, revealing a greater rate of WEB modification of 90.6% compared with previously reported rates of 25%-73% [14,19,32,62] possibly owing to different study designs based on only qualitative methodologies.

The quality of aneurysm occlusion was not correlated with WEB shape alteration, contrary to what Janot et al. had previously observed [35]. The precise mechanism of the shape change of WEB is not yet known. Cognard and Januel [19] classified this problem as a hemodynamic phenomena and proposed that the increased arterial inflow may be causing a water-hammer effect. Using computational fluid dynamics models in a series of 19 aneurysms, Caroff et al. [14] were able to demonstrate a strong correlation between aneurysm flow exposure and shape modification. Furthermore, Pierot [53] regarded WEB shape alteration as a component of a healing process that starts with thrombus development, continues with clot retraction, and ultimately ends with fibrosis or the formation of scar tissue.

The current study's findings revealed that shape alteration could indeed be a healing process because no correlation with occlusion worsening was observed. We noticed that during this process, the WEB device changed shape from an elliptical sphere to a shape that could be compared to a "butterfly shape" (Figure 11C); with the distance between 2 markers being shortened, the markers in the middle represented the trunk, and the bilateral wires that were pushed aside represented the wings.

In the present study, a mixed pattern of continuous device height fall with various slopes was found using time course analysis. In a previous study, Janot et al. [35] quantified the effects of WEB shape alteration on DSA at the end of the intervention and on control angiograms after 6 and 18 months. According to their findings, the majority of shape changes were already apparent at short-term follow-up (6-month DSA) and become more pronounced as time went on until the 18-month control. Due to the vastly disparate CT follow-up timeframes across the patients in our study, it was impossible to discern between different follow-up periods in time. However, because our research contained quantitative data up to a 5.9-year period, our results showed a statistically significant continuing decline of WEB height also beyond the 18-month interval.

In conclusion, with a median yearly decrease rate of 19.2% in height, 90.6% of patients treated with a WEB demonstrated shape alteration of the device during follow-up. The degree of aneurysm occlusion was not related to WEB form alteration.

7- Contour-assisted coiling in wide-necked aneurysms
(Wodarg F, **Özpeynirci Y**… *Interventional Neuroradiology 2022*)

The WEB is the most well-known product in the category of endosaccular flow disruptors. Recurrences are possible, especially in large and partly thrombosed aneurysms [36,38,45,71]. The widest WEB currently on the market has a diameter of 11 mm, hence aneurysms greater

than 10 mm do not constitute a primary indication for treatment with WEB.

The Contour device (Cerus Endovascular, Fremont, CA, USA) is intended to be implanted just at the neck and is designed to cover the neck regardless of the size, shape, or irregularity of the dome. Contour may thus provide a novel strategy to treating aneurysms with challenging dome shape, such as partly thrombosed or large aneurysms. It is meant to be utilized as a single device, stabilizing in the aneurysm neck; however, a second microcatheter could be jailed alongside the Contour to deploy additional coils in the aneurysm. Without using a permanent intraluminal implant in the parent artery, the major objective of this technique is to merge the impact of flow disruption at the aneurysm neck with the effect of coil embolization in the aneurysm sac. Here, either the Contour retains the coils inside an aneurysm or coils are utilized to support the Contour device in situations of a broad neck or partly thrombosed sac.

We reviewed the periprocedural safety, feasibility, and efficacy of the Contour-assisted coiling with jailed-microcatheter-for-better-occlusion method (CoCoJaMBO) in 8 consecutive patients. In two participating centers (Uniklinikum München and Kiel), between October 2018 and December 2020, we retrospectively examined consecutive patients who had endovascular treatment for saccular cerebral aneurysms with a Contour device.
The CoCoJaMBO approach was used to treat all of the patients who were selected and included in this research. Demographic information, clinical presentation, aneurysm features, therapy information, and, if available, clinical follow-up findings were all documented for each patient.

8 patients (5 female) with an average age of 60.1 years were included in this study. There were eight aneurysms: four on the basilar artery tip, two at the bifurcation of the middle cerebral artery, one at the anterior communicating artery and one in the paraophthalmic segment of the left internal carotid artery. The mean dome width was 10.3 mm, the mean average dome height was 12.8 mm, and the mean neck width was 5.5 mm.

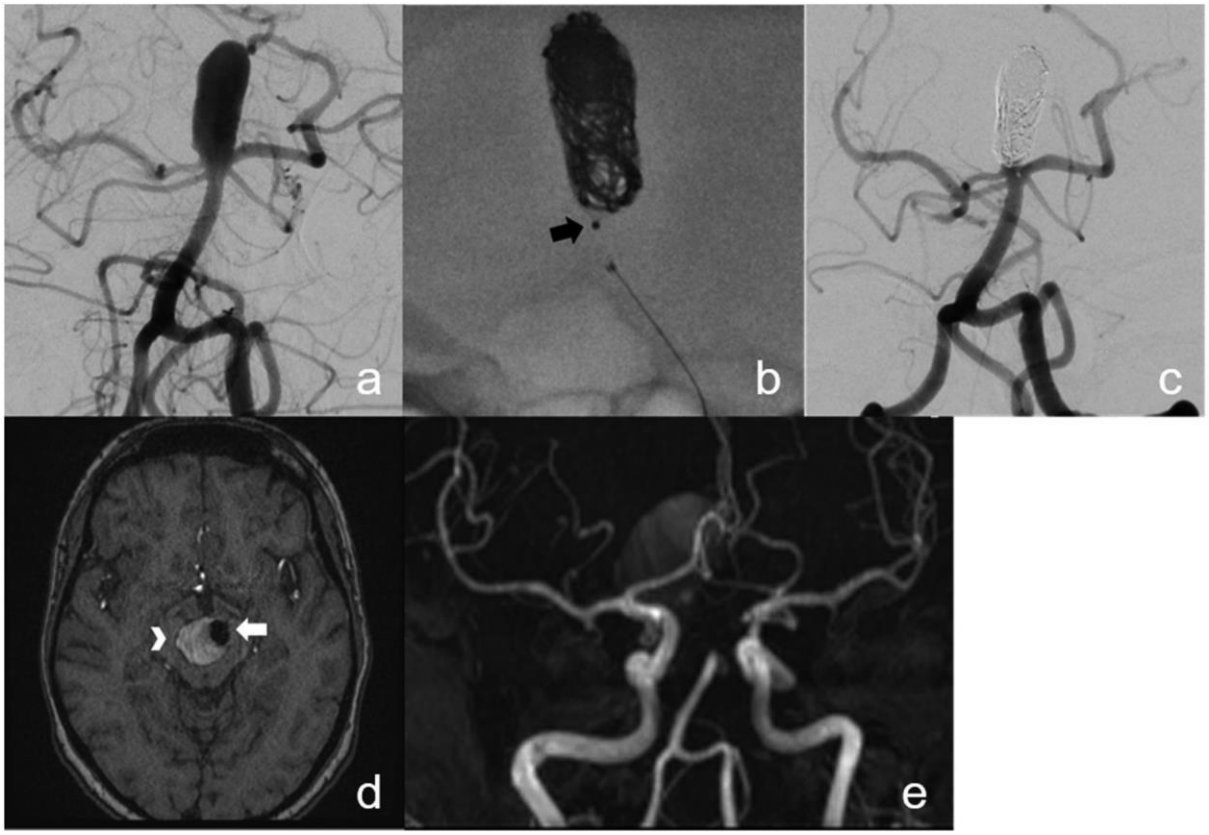

Figure 12 *Patient with partially thrombosed giant basilar tip aneurysm presenting with brainstem compression symptoms (a). CoCoJaMBO was done to create flow disruption at the neck level (black arrow on b) with Contour, stabilized by coils, without having to place a stent in the basilar artery (b, c).*

MRI after 3 months (d, e) shows total aneurysm occlusion.
Reprinted from Contour-Assisted coiling with jailed microcatheter May result in better occlusion (CoCoJaMBO) in wide-necked intracranial aneurysms: Proof of principle and immediate angiographic results*, Wodarg F et al., Interv Neuroradiol. 2022, p. 8.*

There were no procedure-related problems. Five of the eight patients showed immediate aneurysm occlusion. Two patients had residual inflow but significant contrast agent stasis, which is a sign of a successful flow interruption. A small neck remnant was present in just one case.

WEB utilized in combination with coils has previously been reported with limitations [38], as WEB was unable to resist compaction in large and partly thrombosed aneurysms [71]. In light of our limited experience, we think that extra coiling may assist in maintaining the Contour's tight fit to the neck plane, hence encouraging stable occlusion in aneurysms with unfavorable size and neck width without the requirement for persistent antiplatelet medication.

We suggest that the extra coil embolization used in the CoCoJaMBO approach offers adequate protection against rebleeding, similar to stent-assisted coiling.

A combination of endosaccular flow disruption and intra-aneurysmal coil occlusion without the need for long-term antiplatelet medication, in our opinion, adds value to the currently available treatment options for wide-necked bifurcation aneurysms, particularly for very large and complex aneurysms, while minimizing the complexity of the procedure itself.

8- Neqstent coil-assisted flow diverter for treatment of bifurcation aneurysms
(Liebig T…**Özpeynirci Y…**Fiehler J. *Journal of Neurointerventional Surgery 2023*)

Coiling alone has shown limitations in the treatment of wide-necked aneurysms, including high rates of incomplete occlusion, aneurysm recurrence, and an increased risk of coil protrusion into the parent artery, potentially leading in thromboembolic complications [75].

Coiling with stent assistance addressed the problems of stand alone-coiling and has been associated with increased packing density and a lower recurrence rate, but also with a higher rate of major complications [33,57]. Moreover, the requirement of long-term antiplatelet therapy for stent patency complicates the treatment of ruptured aneurysms in acute phase [49].

Neqstent, introduced in 2018, is a woven self-expanding device with a cup-like shape covering the neck, allowing crossing of the microcatheter for coiling after deployment and at the same time exhibiting flow-disrupting qualities (Figure 13). Although its use has already been described in the series by Diana et al. [22], we conducted the first single-arm, prospective, multi-center trial to evaluate the safety and efficacy of NQS for unruptured wide-neck bifurcation aneurysms at six centers across Europe (Austria, Denmark, Germany, and Switzerland) and Canada.

Figure 13 *Illustration of the Neqstent coil-assisted flow diversion (NQS) in a wide-necked bifurcation aneurysm. The aneurysm and vessel contours are indicated by dashed lines. From left: The*

microcatheter and microwire are seen passing through the expanded device at the neck level. Following removal of the microwire, coiling of the aneurysm continued with adequate neck protection.
Reprinted from Neqstent coil-assisted flow diverter (NQS) for the treatment of bifurcation aneurysms: the coil-assisted flow diversion safety and performance study (CAFI), *Liebig T et al., J Neurointerv Surg. 2023, p. 2*.

Technical success, aneurysm occlusion on six-month angiographic follow-up, and mortality or incidence of a major stroke within 30 days/6 months constituted the study's primary endpoints. Procedure time, the quantity of deployment attempts, and the rate of re-treatment were secondary endpoints.

Angiographic images before and after the intervention, as well as follow-up images were evaluated using the Raymond-Roy Scale (Figure 7) and a modified version of the Bicetre refined WEB Occlusion Scale [15].

Intention-to-treat (ITT) group consisted of 38 and per-protocol (PP) group consisted of 36 patients. In two cases device deployment was technically not possible (5.3%).

Device-related adverse events were reported in 4/38 (10.5%) patients, one hemorrhagic (aneurysm rupture) and three thromboembolic, with one patient suffering a debilitating stroke due to a thromboembolic complication with persisting symptoms at 6 months.

An adequate occlusion, as defined above, was observed in 9/36 patients immediately following the intervention (25%) and increased to 31/36 (86.2%) at 6 months. Complete occlusion rate on the last available angiography (median 6 months) was 80.6%.

The results of this study proved the safety and efficacy of this technique compared to other techniques used in treatment of wide-necked bifurcation aneurysms. The device safety was found at least comparable to the stent-assisted coiling, but inferior to WEB.

Regarding efficacy, the occlusion rates were better than those described in the series with other treatment techniques, including microneurosurgery [25].

The results of our study emphasize the following properties of this device: its potential as an endosaccular flow disruptor, combination with coiling, allowing to re-cross in case the position of the coiling microcatheter is lost, and no need for long-term antiplatelet therapy.

Further research is required to accurately position this novel instrument within the current array of technologies utilized in the treatment of aneurysms.

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