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Original research

CLinical EValuation of WEB 17 device in intracranial aneuRysms (CLEVER): procedural, 30-day and 1-year safety results for ruptured and unruptured aneurysms

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ABSTRACT

Background Intrasaccular flow disruption is an endovascular approach for the treatment of wide-neck aneurysms and, more specifically, wide-neck bifurcation aneurysms, which are challenging to treat with previously developed technologies. The Woven EndoBridge (WEB) device has demonstrated its efficacy and safety, for both unruptured and ruptured aneurysms.

Methods The CLEVER study was an observational, multicenter, prospective study conducted in 17 European investigational sites using the WEB 17 device, for the treatment of ruptured and unruptured aneurysms. The study objective was to provide safety and efficacy data on the WEB 17 device in the treatment of wide-neck bifurcation aneurysms. Imaging results were assessed independently by a Corelab and adverse events adjudicated by a Clinical Event Adjudicator. This analysis reports procedural results and safety at 30 days and 12 months.

Results A total of 163 patients (mean age 58.1 years; 68.1% women) with 103 unruptured aneurysms and 60 ruptured aneurysms were enrolled. Most aneurysms were located on the anterior communicating artery (ACom) (37.4%) or the middle cerebral artery (MCA) bifurcation (30.1%). Aneurysm widths ranged from 2.0–9.2 mm, and the mean sac width was 5.0 mm. The WEB procedure was successfully completed in 163 patients (100%). At the 12-month follow-up, major stroke events occurred in 3 of 163 patients (1.8%), and no device-related mortality was observed.

Conclusion Endovascular treatment of ruptured and unruptured wide-neck bifurcation aneurysms using WEB 17 is safe, with a low complication rate and no device-related mortality. In particular, none of the ruptured aneurysms bled again up to 1 year of follow-up.

Trial registration number NCT03844334.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The Woven EndoBridge (WEB) device has been evaluated for over 10 years for the endovascular treatment of wide-neck bifurcation aneurysms, both ruptured and unruptured. Its safety and efficacy have been demonstrated.

WHAT THIS STUDY ADDS

⇒ WEB 17 is an important evolution of the WEB design. It can be inserted into 0.017 inch catheters.

⇒ This study shows that at 1 month and 1 year, WEB 17 retains the same excellent level of safety and efficacy against bleeding as previous generations.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This technological evolution enables the treatment of smaller, more distal aneurysms, whether unruptured or ruptured.

⇒ This analysis confirms the good efficacy of WEB treatment of ruptured wide-neck aneurysm, which might induce further adoption in real life practice.

INTRODUCTION

The Woven EndoBridge (WEB; Microvention, Aliso Viejo, CA) device is an intrasaccular flow disruptor that has been specifically developed for the treatment of wide-neck bifurcation aneurysms.[1 2] In its development, WEB has evolved from a double chamber design (WEB-DL) to a single chamber design (WEB-SL), allowing for a smaller delivery catheter, while keeping the same level of safety and effectiveness.[3] WEB has been evaluated in numerous multicenter prospective studies, and retrospective series conducted worldwide on both ruptured and unruptured aneurysms.[4–10] The latest evolution of WEB, the WEB 17 device, has made it possible to deliver the implant through a 0.017 inch microcatheter. This represents an improvement in

ease of use.[11] This miniaturization comes at the cost of a reduction in the number of wires (from 144–216 wires in WEB 21 to 72–108 in WEB 17) and wire diameter, and it is essential to demonstrate that WEB 17 will maintain the same level of safety and effectiveness as the previous generation of WEB. This is the purpose of the CLEVER (CLinical EValuation of WEB 17 device in Intracranial AneuRysms) study. To date, only limited series have recently described the use of the new WEB 17.[12–14] In this article, we report the procedural, 30-day, and 1-year safety results of the CLEVER study, which was conducted at 17 sites in Europe.

METHODS

Study design

The CLEVER study is a prospective, single-arm, multicenter, observational clinical study conducted in 17 centers in Hungary, Finland, France, Germany and the UK. The study enrolled patients with unruptured and ruptured aneurysms of the anterior and posterior intracranial circulations.

The CLEVER study is registered in ClinicalTrial.gov under NCT03844334, and funded by Microvention. It received all national regulatory approvals in accordance with local regulations. All patients signed an informed consent form for their personal data processing, authorizing their anonymized medical records to be sent to the clinical event adjudicator (CEA) and Corelab and allowing the monitors to check the medical records against the electronic case report form (eCRF) data. Patients were informed that no changes were made to the treatment they received and that they could withdraw their consent at any time. Patient data were collected according to the International Conference on Harmonization Guideline for Good Clinical Practice (GCP) requirements.

Inclusion criteria at baseline were patients aged 18 to 80 years with an unruptured or ruptured intracranial saccular bifurcation aneurysm. According to the study protocol, only patients having one aneurysm requiring treatment were eligible. A ruptured aneurysm patient was defined as a patient with CT, MRI, or lumbar puncture evidence of subarachnoid hemorrhage (SAH) attributed to the index aneurysm within the last 30 days. The diameter and height of the aneurysm had to be an appropriate size for treatment with the WEB 17 device (WEB width available between 3 and 7 mm). The decision to treat and the method of treatment was determined independently of the study during a local multidisciplinary meeting including neurosurgeons and neuroradiologists according to each site's practice.

Patients with ruptured aneurysms had to have a Hunt and Hess score ≤III.

Study endpoints

The primary safety endpoint is the proportion of patients with death of any non-accidental cause or any major stroke (defined as an ischemic or hemorrhagic stroke resulting in an increase of ≥4 points on the National Institutes of Health Stroke Scale) within the first 30 days after treatment, or major ipsilateral stroke or death due to neurologic cause from day 31 to 1 year after treatment. The primary safety endpoint is presented in this article.

Secondary endpoints presented here include technical success, morbidity rate defined as the proportion of patients with modified Rankin Scale (mRS) >2 (if baseline mRS was <2) or an increase of at least one point if ruptured aneurysm or if baseline mRS ≥2, per-procedural adverse events, neurological and neurovascular complications, and aneurysm rupture and re-rupture rates.

The primary efficacy endpoint, not presented in this paper, includes an adequate occlusion rate with no retreatment at the 12-month follow-up. Secondary efficacy endpoints include complete occlusion rate, recurrence or recanalization rate, and retreatment rate also at 12 months.

Procedure

The embolization procedure was performed under similar conditions as those for standard coiling. The aneurysm was catheterized with a VIA 17 microcatheter (MicroVention, Aliso Viejo, CA). The decision on which form of WEB (barrel shape, referred to as 'WEB SL', and sphere shape, referred to as 'WEB SLS') to use was determined by the operator.

The WEB 17 device was intended to be used alone as a first-line treatment for the target aneurysm. The use of additional devices was allowed based on the individual interventional neuroradiologist's decision. Antiplatelet therapy was used according to the standard of care and was recorded at each visit. Endovascular treatment and follow-up evaluations were performed as per the standard of care.

Regarding ruptured aneurysms, there was a specifically strict protocol:

1. To ensure that there was no bleeding between the initial diagnosis of SAH and WEB placement, a new CT scan (conventional or flat panel) was systematically redone either in case of clinical worsening or systematically after the possible placement of an external ventricular shunt.
2. To ensure the detection of any hemorrhage that occurred after WEB placement up to 1 month after treatment, it was recommended that a flat-panel CT scan should be performed in the angiosuite at the end of treatment, and an unenhanced CT or MRI scan should be performed again for any change in the patient's neurologic status up to 1 month after the procedure.

Data collection and analysis

All data were collected in an electronic eCRF and independently monitored by a clinical research organization. To minimize bias, a Corelab assessed efficacy endpoints, and all adverse events were adjudicated by a CEA. This safety analysis was performed based on the intention-to-treat population consisting of patients who were enrolled and underwent at least one attempt of treatment with a WEB 17 device (defined as when the WEB device was inserted into the delivery catheter when the catheter was in place).

Statistical analysis

This article reports the study design, patient demographics, procedural characteristics, and 30-day and 1-year safety outcomes. The study was based on the Objective Performance Criterion (OPC)[15] for efficacy and safety and used a standard frequentist approach to conduct statistical analyses. Descriptive statistics, mean, standard deviation, number evaluated, median, minimum and maximum were presented for continuous baseline characteristics. Categorical variables, numbers evaluated, and percentages were presented for each characteristic as appropriate. The missing data were not replaced and were considered as missing. All data analyses were performed using SPSS version 22.0 (IBM Corp, Armonk, NY).

RESULTS

Between March 2019 and February 2021, a total of 163 patients were enrolled in 17 European interventional neuroradiology

Table 1 Patient baseline characteristics according to aneurysm presentation

	Unruptured group (n=103)	Ruptured group (n=60)	Total (n=163)
Patient baseline characteristics			
Age (years), mean±SD (range)	59.14±10.1 (32–80)	56.25±11.0 (30–75)	58.1±10.5 (30–80)
Women, n (%)	73 (70.9%)	38 (63.3%)	111 (68.1%)
Smoking	49 (47.6%)	26 (43.3%)	75 (46.0%)
Current	12 (24.5%)	4 (15.4%)	16 (21.3%)
Past	37 (75.5%)	22 (84.6%)	59 (78.7%)
Main medical history			
Systemic hypertension	53 (51.5%)	30 (50.0%)	83 (50.9%)
Hyperlipidemia	20 (19.4%)	7 (11.7%)	27 (16.6%)
Diabetes mellitus	9 (8.7%)	2 (3.3%)	11 (6.7%)
mRS score			
0	83 (80.6%)		
1	17 (16.5%)		
2	1 (1.0%)		
3	2 (1.9%)		
Hunt and Hess score			
I		16 (26.7%)	
II		32 (53.3%)	
III		12 (20.0%)	
Aneurysm baseline characteristics and procedural information			
Aneurysm, maximum sac width (mm)			
Mean±SD	5.1±1.3	4.8±1.7	5.0±1.4
Range	2.5–8.9	2.0–9.2	2.0–9.2
Aneurysm maximum neck size (mm)			
Mean±SD	3.6±0.9	3.3±0.9	3.5±0.9
Range	1.8–6.7	1.5–5.7	1.5–6.7
Dome to neck ratio			
<2	99 (96.1%)	57 (95.0%)	156 (95.7%)
≥2	4 (3.9%)	3 (5.0%)	7 (4.3%)
Aneurysm location			
ACom complex	32 (31.1%)	29 (48.3%)	61 (37.4%)
MCA bifurcation	37 (35.9%)	12 (20.0%)	49 (30.1%)
PCom	5 (4.9%)	12 (20.0%)	17 (10.4%)
Basilar apex	11 (10.7%)	3 (5.0%)	14 (8.6%)
Pericallosal artery/ACA	6 (5.9%)	1 (1.7%)	7 (4.3%)
ICA terminus	5 (4.9%)	1 (1.7%)	6 (3.7%)
Other	7 (6.8%)	2 (3.3%)	9 (5.5%)
MCA M1*	3 (2.9%)	0 (0.0%)	3 (1.8%)
PICA	1 (1.0%)	1 (1.7%)	2 (1.2%)
Posterior cerebral artery	1 (1.0%)	0 (0.0%)	1 (0.6%)
Basilar trunk	1 (1.0%)	0 (0.0%)	1 (0.6%)
Carotid ophthalmic artery*	1 (1.0%)	0 (0.0%)	1 (0.6%)
Superior cerebellar artery*	0 (0.0%)	1 (1.7%)	1 (0.6%)

*Aneurysms located on MCA M1, carotid ophthalmic artery and superior cerebellar artery were classified as bifurcation at a branch, instead of usual bifurcation definition.
ACA, anterior cerebral artery; ACom, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale; PCom, posterior communicating artery; PICA, posterior inferior cerebellar artery.

centers. Sixty patients presented with a ruptured aneurysm and 103 with an unruptured aneurysm.

Patient and aneurysm characteristics

Patient characteristics are summarized in table 1. Most patients with unruptured aneurysms had an mRS ≤2 (101/103; 98.1%). Two patients had an mRS of 3: one with no neurological history, and one with motor disorders due to multiple sclerosis.

The 163 patients were treated for 163 aneurysms; 36 patients had multiple aneurysms, including 11 patients in the ruptured group, and only one aneurysm per patient was treated during the index procedure.

As assessed by the Corelab, the mean sac width of unruptured aneurysms was 5.1 mm (range 2.5–8.9 mm), and 4.8 mm (range 2.0–9.2 mm) for ruptured aneurysms (table 1). The sac width was consistent with the recommended size for use of the WEB 17; 95.0% of the ruptured aneurysms were broad-based (dome-to-neck ratio <2), and 96.1% of the unruptured aneurysms. Anterior communicating artery (ACom) and middle cerebral artery (MCA) aneurysms represented the majority of the treated aneurysms.

Procedural results

The WEB 17 procedure was successfully completed in all aneurysms (163/163, 100%); 143 aneurysms were treated with WEB SL (87.7%) and 20 with WEB SLS (12.3%).

In most cases (137 patients; 84.0%), the WEB device was successfully implanted in the target aneurysms on the first attempt (81.6% and 88.3% in unruptured and ruptured aneurysm groups, respectively). For 23 patients (14.1%), a second attempt was necessary, and for three patients (1.8%), the attempt with a third WEB was successful.

An adjunctive balloon was used to assist WEB positioning in 10/163 cases (6.1%). Implantable adjunctive devices were used in 6/163 cases (3.7%): a stent in three unruptured aneurysms, coils in two ruptured aneurysms, and coils plus a stent in one unruptured aneurysm.

The mean fluoroscopy time was 27.8 min (range 5.9–151.0 min).

Antiplatelet regimen

Among the unruptured population, 83.5% of the patients received at least one antiplatelet premedication, whereas among the ruptured population, 93.3% of the patients did not receive any antiplatelet premedication. The antiplatelet regimens used are shown in table 2.

Primary safety endpoint

The primary safety endpoint as defined above has been adjudicated by the CEA (table 3). Four events occurring in three patients (1.8%) met the primary safety endpoint. All these events were major ischemic strokes, two in the same patient with an unruptured aneurysm (1/103; 1.0%) and the two others in two patients with ruptured aneurysms (2/60; 3.3%).

The first patient (patient A) with an unruptured left MCA bifurcation aneurysm had two events, right hemiparesis and dysarthria, both occurring the day after the procedure and

Table 3 Safety results based on the CEA adjudicated complications until 1 year

	Unruptured group	Ruptured group	Total
Primary safety endpoints	1* (1.0%)	2 (3.3%)	3 (1.8%)
Overall mortality			
At 30 days	0 (0%)	0 (0%)	0 (0%)
Device-related†	0%	0%	0%
At 1 year	1 (1.0%)	0 (0%)	1 (0.6%)
Device-related†	0%	0%	0%
Overall morbidity			
At 30 days	0 (0%)	9 (15.8%)	9 (5.7%)
Device-related†	0%	1 (1.7%)	1 (0.6%)
At 1 year	0 (0%)	3 (5.5%)	3 (2.0%)
Device-related†	0%	0%	0%
Peri-procedural events			
Thromboembolic events‡	3 (2.9%)	7 (11.7%)§	10 (6.1%)
Device-related†	3 (2.9%)	6 (10%)	9 (5.5%)
Per-operative rupture	–	1 (1.7%)	1 (0.6%)
Device-related†	0%	1 (1.7%)	1 (0.6%)
Dissection	1 (0.9%)	1 (1.7%)	2 (1.2%)
Neurological events due to initial disease	1 (0.9%)	2 (3.3%)	3 (1.8%)
Non-neurological events	2 (1.9%)	3 (5.0%)	5 (3.1%)
Device-related†	0%	0%	0%
Post-procedural neurological events with clinical impact at 30 days			
Vasospasm	–	2 (3.3%)	2 (1.2%)
Hydrocephalus	–	1 (1.7%)	1 (0.6%)
Seizures	–	1 (1.7%)	1 (0.6%)
Visual impairments (Terson syndrome)	–	1 (1.7%)	1 (0.6%)

*One patient had two major strokes meeting the primary safety endpoint (one before 30 days and one between 31 days and 1 year).
†Defined by the CEA as 'device-related' or 'device and procedure-related'.
‡Thromboembolic events include ischemic stroke, thrombosis branch/parent artery, and hemiparesis due to protrusion.
§One event (major ischemic stroke) included in the primary endpoint events.
CEA, clinical event adjudicator.

Table 2 Antiplatelet regimen before and after the WEB procedure according to aneurysm presentation

	Unruptured				Ruptured			
Number of antiplatelet medications	Pre-procedure n=103	On the day of the procedure n=103	30 days n=103	1 year n=97	Pre-procedure n=60	On the day of the procedure n=60	30 days n=60	1 year n=56
0	17 (16.5%)	11 (10.7%)	31 (30.1%)	58 (59.8%)	56 (93.3%)	41 (68.3%)	43 (71.7%)	46 (82.1%)
1	25 (24.3%)	29 (28.2%)	57 (55.3%)	33 (34.0%)	3 (5.0%)	17 (28.3%)	13 (21.7%)	6 (10.7%)
2	59 (57.3%)	62 (60.2%)	15 (14.6%)	6 (6.2%)	1 (1.7%)	2 (3.3%)	4 (6.7%)	4 (7.1%)
3	2 (1.9%)	1 (1.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0.0%)	0 (0%)	0 (0%)

both associated with ischemic lesions in the left MCA territory. Control angiography showed a WEB device protrusion that led to a Y-stenting rescue procedure, and the event was adjudicated as a major device-related stroke. After the procedure, the issue was resolved without any sequelae; at discharge, the patient's mRS was 0. Another event occurred at 1 year consisting of an ischemic stroke after the discontinuation of aspirin. This event was adjudicated as related to the stent-rescue procedure and resolved without sequelae.

The second patient (patient B) with a ruptured ACom aneurysm had a left pericallosal artery thrombosis due to difficult catheterization, managed with intraprocedural antiplatelet treatment. The event was adjudicated as a major procedure-related stroke. They also had a right interhemispheric hematoma and hydrocephalus, both secondary to initial disease. The patient's mRS was 5 at the 30-day follow-up and 4 at 1 year.

The third patient (patient C) with a ruptured ACom aneurysm had paroxysmal atrial fibrillation on the day of the procedure which resulted in multiple supratentorial ischemic lesions. The event was adjudicated as a major stroke related to a concomitant condition (heart disease) and resulted clinically in right hemiplegia. The patient's mRS score was 4 both at discharge and at the 4 months follow-up.

Based on the success criteria defined according to the OPC approach, the primary safety endpoint was met for the ruptured and unruptured groups as detailed below:

- Ruptured group: The rate of safety events is 3.3% in the study. The significance level test that the rate is lower than 23.1% resulted in $P<0.001$. The higher bound of the two-sided 95% confidence limit of 11.5% exceeds the 23.1% performance goal.
- Unruptured group: The rate of safety is 1.0% in the study. The significance level test that the rate is lower than 14.1% resulted in $P<0.001$. The higher bound of the two-sided 95% confidence limit of 5.3% exceeds the 14.1% performance goal.

Mortality and morbidity rates

Throughout the study, nine patients were lost to follow-up: four patients between 1- and 6-month follow-up, and five patients between 6- and 12-month follow-up (table 3).

At 1 month, 159 patients had a clinical status assessed using mRS. At 1 month, nine morbidities were reported. One was adjudicated as device- and procedure-related with the patient presenting an mRS of 3. One was procedure-related with an mRS of 5 (patient B described above). Six were adjudicated as being a consequence of the initial aneurysm rupture, with four patients presenting an mRS of 4 and two patients an mRS of 3. The events associated were vasospasm, hydrocephalus, seizures, or visual impairment. One was related to concomitant disease (cardiac) with an mRS of 4 (patient C described above).

At 1 year, 151 patients had a clinical status assessed using mRS, while for three patients, only proof of life could be formally obtained by telephone (mRS could not be assessed due to the COVID pandemic). Thus, morbidity and mortality rates were assessed on 151 and 154 patients, respectively. At 1 year, among the three patients with morbidity, two of them are already reported at 1 month (patients B and C), and the third patient was adjudicated as related to polyneuropathy and vertebral body fractures with an mRS of 3.

Overall morbidity rates at 1 month and 1 year were 9/159 (5.7%) and 3/151 (2.0%), respectively, all occurring in patients with ruptured aneurysms.

Overall mortality rates at 1 month and 1 year were 0% and 0.6% (1/154), respectively. One patient with a ruptured aneurysm died 3 months after the procedure due to cardiac disease.

Peri-procedural adverse events

A total of 21 peri-procedural events (occurring the day of the procedure), with or without clinical consequences, were recorded in 19 patients (11.7%); 81% (17/21) of the events were without clinical consequence (table 3).

Among the 21 peri-procedural events, 10 (6.1%) were adjudicated as device- or device- and procedure-related events with one presenting clinical consequences: nine were thromboembolic (six ruptured group/three unruptured group); one had clinical impact (1/163; 0.6%) and concerned a patient (patient D) treated for a non-ruptured aneurysm who suffered hemiparesis due to WEB protrusion after detachment, leading to stenting of the aneurysm. mRS was 1 both at discharge and at 6 months follow-up.

One (0.6%) peri-operative rupture occurred in a patient treated for a ruptured aneurysm. It had no clinical consequences and the complication is described in the per-operative rupture section).

Eleven events were adjudicated as not related to the device. One thromboembolic event, with clinical consequences, was adjudicated as procedure-related (see patient B). There were two dissection events (1.2%). The first (patient E) was incidentally discovered at the carotid siphon on a systematic follow-up performed 9 days after the treatment of a ruptured left MCA aneurysm. It was attributed to the 5 French (5F) Sofia guiding catheter used in conjunction with a short 5F sheath. The patient was stented and resulted in visual acuity reduction of the patient's left eye with patient mRS 1 both at discharge and at 1 year follow-up. The second event had no clinical consequences. Three neurological events due to initial disease occurred: two hydrocephalus (1.2%), both in patients treated for a ruptured aneurysm, without clinical consequence; one gaze deviation (0.6%) occurred in a patient treated for a non-ruptured aneurysm that was adjudicated as being related to the study disease condition and resolved without sequelae. Five non-neurological events included access site complications in two patients (1.2%), cardiac events in two patients (1.2%), and infection in one patient (0.6%). These events resolved without sequelae with the exception of patient C.

Post-procedural neurological complications occurring up to 30 days

Thirty-six post-procedural (occurring after the day of the procedure) neurological events were reported (table 3). These events occurred in 31 patients (19.0%), three with an unruptured aneurysm (3/103; 2.9%), and 28 with a ruptured aneurysm (28/60; 46.7%). Two were adjudicated as device- or device- and procedure-related events and had no clinical consequences. One patient (patient F) with a ruptured Acom aneurysm had a transient ischemic attack (transient paresthesia and paresis left arm) the day after the procedure. MRI showed emboli infarction in the right anterior cerebral artery territory. The event was adjudicated as possibly related to the device and the procedure, and resolved without sequelae. The other event corresponds to patient A.

Among the 36 events, five (3.1%) had clinical consequences at 30 days (table 3): two vasospasms, one hydrocephalus, one visual impairment, and one seizure. They all occurred in patients

with ruptured aneurysms and were adjudicated as related to the study disease condition.

Ruptures and rebleeds

Protection against rebleeding

Of the 60 patients who underwent emergent treatment for a ruptured aneurysm, none experienced aneurysm rebleed from post-procedure up to 1 year.

Peri-operative rupture

There was one (0.6%) per-operative aneurysm rupture that occurred in a patient treated for a ruptured posterior communicating artery (PCom) aneurysm that was detected during the angiographic control performed after WEB deployment. A balloon was immediately inflated for 2 min in front of the neck of the aneurysm, and the bleeding stopped. Bleeding in the interpeduncular cistern without intra-parenchymal hematoma was confirmed by peri-operative CT scan. The patient had no clinical consequences and the event was adjudicated as a device-related SAH.

Hemorrhagic complication

One patient treated for an unruptured right MCA bifurcation aneurysm presented with a headache 6 days later, and CT demonstrated an SAH in the right frontal sulcus. A follow-up angiogram confirmed complete exclusion of the aneurysm by the WEB device during the index procedure. The SAH was adjudicated as being related to the procedure and the study's disease. The patient's mRS was 0 both at the 1-month and 1-year follow-up.

DISCUSSION

The WEB 17 is the latest evolution in WEB technology, developed to enable it to be used in 0.017 inch catheters (ie, with diameters as small as those used to coil aneurysms). The expected benefit is to improve the ease of use and allow more distal navigation with the VIA 17 microcatheter, compared with the use of VIA 21 catheters. To enable this technological evolution, it has been necessary to modify the WEB structure, in particular the number and diameter of the wires.[11] It is important to ensure that these modifications retain not only the same safety as the WEB 21 but also the same effectiveness in aneurysmal occlusion.

Van Rooij *et al*,[13] Mihalea *et al*[11] and Goertz *et al*[16] were the first to report their experience of WEB 17 in single-center studies. The current study, CLEVER, is the first controlled multicenter study to investigate WEB 17 in routine use during the treatment of both unruptured and ruptured aneurysms.

In the CLEVER study, WEB 17 was successfully deployed in 100% of patients with a short fluoroscopy mean time of 27.8 min.

All kinds of peri-operative adjunctive devices were used in 10.0% of cases, whereas they were used in 4.1% in WEB IT,[17] 5.4% in CLARYS[8] and 9.2% in the three GCP studies.[5] One potential explanation is the increasingly widespread use of balloons by operators due to their better understanding of the WEB, which has led them to broaden its indications. In CLEVER, for example, all balloons were used to help position the WEB.

Stents were used in six patients (3.7%), peri-operatively in four patients or soon after the index procedure in two patients, leading to clinical consequences in three patients (patients A, D and E). In a single center study, Sahnoun *et al*[18] reported use of stenting in conjunction with WEB in 12.1% of cases without morbi-mortality, almost all of them (18/19) due to WEB protrusion.

In our series, considering WEB protrusion, additional stenting was required for three patients (1.8%), all unruptured. Comparatively, in the three GCP studies,[5] protrusion was observed in 4.1% of aneurysms, managed by WEB removal in two patients (2/169, 1.2%) and stenting in 3.1% of aneurysms treated by WEB; whereas in WEB IT,[17] stenting was used because of protrusion in 1.4%.

ACom and MCA aneurysms represented the majority of the aneurysms treated (68.3% in the ruptured group vs 67.0% in the non-ruptured group), but their proportions differed between the two groups: MCA bifurcation aneurysms were more frequently encountered in the group of unruptured aneurysms than in ruptured aneurysms (35.9% and 20.0%, respectively), whereas ACom aneurysms were more frequently encountered in the group of ruptured aneurysms than in unruptured aneurysms (48.3% and 31.1%, respectively).

Due to the use of VIA 17 and WEB 17, more difficult to reach aneurysms were able to be treated, such as more distal aneurysms (11 patients; 6.7%: pericallosal, posterior cerebral, superior cerebellar, and posterior inferior cerebellar artery arteries) and side-wall aneurysms (22 patients; 13.5%: PCom, MCA M1 segment, basilar trunk, and carotid ophthalmic segment). The difficulty in the treatment of these types of aneurysms has been discussed further in Zimmer *et al*.[19]

A dome-to-neck ratio <2, indicating broad-based anatomy, was observed in 95.7% of cases in this study and successfully treated with the WEB device. This confirms the advantage of the WEB in treating these types of aneurysms, which are reputedly difficult using the traditional coiling technique, even with the aid of the balloon remodeling technique.

WEB 17 confirms the safety results achieved for WEB over 10 years. In the treatment of unruptured aneurysms, the current study reports a mortality rate of 0% at 1 month, identical to WEB-IT[17] and the three pooled GCP studies[5] (French Observatory, WEBCAST and WEBCAST-2). At 1 year, the current study reported an unruptured aneurysm mortality rate of 1.0%, compared with 2.7% in WEB-IT[6] and 3.3% in the three pooled GCP studies.[5]

The unruptured morbidity rate in the current study was 0% at 1 month and 1 year, comparable to the rates reported in WEB-IT (0.7% and 1.4%, respectively) and in the three pooled GCP studies (3.0% and 1.3%, respectively).

For the treatment of ruptured aneurysms, the mortality rate for CLEVER was 0% at 1 month and 1 year, compared with 1.7% and 3.8%, respectively, in CLARYS, although the reason for this difference cannot be explained. The morbidity rate for CLEVER ruptured aneurysms was 15.8% at 1 month and 5.5% at 1 year, compared with 15.0% and 9.6%, respectively, in CLARYS.

Peri-procedural thromboembolic events, with or without clinical consequences, were significantly higher in the ruptured group (7/60; 11.7%) versus the unruptured group (3/103; 2.9%) (P=0.039). This trend is similar to the CLARYS study, with a thromboembolic complication rate of 16.7%.[8] The elevated rate of thromboembolic complications during endovascular treatment of ruptured aneurysms is well known and has been reported in other studies as well (eg, 13.3% in CLARITY[20] and 10.4% in ARETA).[21] In ARETA, thromboembolic complications were more frequent in aneurysms located on the bifurcation of the MCA (18.5% vs 8.3% for other locations).

Despite its lower profile, WEB 17 also protects against early rebleeding of ruptured aneurysms: 0% rebleeding at 1 month and 1 year in CLEVER, identical to CLARYS,[8] which specifically

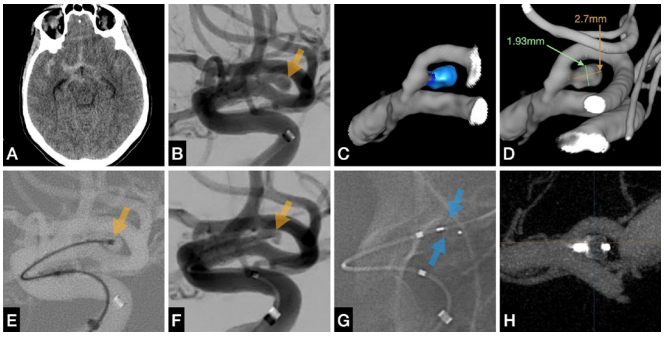

Figure 1 Patient in their 40s presenting with sudden headache, vomiting followed by an epileptic seizure. WFNS 1. mRS 0. (A) NECT showing diffuse subarachnoid hemorrhage predominantly on the right. Fischer 2. (B) Diagnostic DSA showing a ruptured saccular aneurysm of the right MCA bifurcation. (C, D) Small ruptured aneurysm measuring 1.93 mm in diameter and 2.7 mm in height. (E) Tip of VIA 17 microcatheter (arrow) in the aneurysm sac. (F, G) Deployment of a 3x2 mm WEB SL. DSA control before detachment. The arrows show the base of the WEB. (H) Postoperative VasoCT showing detached 3x2 mm WEB SL in the aneurysm. DSA, digital subtraction angiography; MCA, middle cerebral artery; mRS, modified Rankin Scale; NECT, non-contrast enhanced CT; WEB SL, Woven EndoBridge Single Layer; WFNS, World Federation of Neurosurgical Societies.

evaluated the use of WEB 21 in preventing rebleeding of ruptured aneurysms.

Not only can WEB 17 be delivered through smaller profile catheters but it is also available in smaller sizes (3 and 4 mm) and in half sizes (3.5 and 4.5 mm), enabling its use in more distal and smaller aneurysms. With the use of WEB 17, very small aneurysms have been treated, with the smallest ruptured aneurysm treated in this study measuring 2.0 mm (figure 1), whereas in CLARYS, the smallest measured 3.5 mm.

Limitation

A limitation of this study is the lack of a control group. However, many studies on WEB are published and the results of the CLEVER study can be compared with other prospective GCP studies with the same design (WEBCAST, WABCAST-2, French Observatory, CLARYS, WEB-IT). In addition, assessment bias for the primary safety endpoint was minimized by the CEA independent assessment.

CONCLUSION

This multicenter prospective clinical study showed that the WEB 17 device has a low complication rate and is a safe treatment option for unruptured and ruptured wide-neck bifurcation aneurysms. In addition, WEB 17 enables even more distal and/or small aneurysms at difficult bifurcations to be treated. It is essential to confirm this encouraging clinical efficacy by assessing angiographic efficacy at 1 year, which is currently being evaluated.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The study received national regulatory authorization following each country's requirement: In France the study was approved by the national ethics committee (CPP Ouest IV – Nantes) and declared to the CNIL (National Commission for Information Technology and Civil Liberties). In Germany the study was approved by the local ethics committee of each participating center except Heidelberg which did not require a new submission. The ethics committees are: Ethikkommission der Bayerischen Ländesärztkammer, Ruhr Universität Bochum Ethik-Kommission der Medizinischen Fakultät, Ländesärztkammer Thüringen, Ethik-Kommussion der Arztekammer Hamburg, Medizinische Fakultät der Christian-Albrechts-Universität zu Kiel, Ethikkommission bei der LMU München. In Hungary the study was approved by the local ethics committee. In Finland the study was approved by the local ethics committee of each participating center: Varsinais-Suomen Sairaanhoitopiiri (Turku) and Helsingin Ja Uudenmaan Sairaanhoitopiiri (Helsinki). In the UK the study was approved by the national ethics committee (Yorkshire & the Humber – Bradford Leeds Research Ethics Committee). Participants gave informed consent to participate in the study before taking part.

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