Case series

The ARTISSE intrasaccular device for intracranial aneurysm treatment: short-term, mid-term and long-term clinical and angiographic results

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ABSTRACT

Background The concept of intra-aneurysmal flow disruption has emerged as a new paradigm for the treatment of primarily bifurcation aneurysms. The purpose of this study was to determine the clinical and angiographic outcomes of patients treated with the new ARTISSE intrasaccular device (ISD).

Methods Selected patients with bifurcation aneurysms that matched the indications of the ARTISSE ISD defined by the manufacturer were treated in a single center. Clinical and angiographic follow-up was conducted at 6 and 36 months. Aneurysm occlusion was assessed using the Raymond–Roy classification scale.

Results Nine subjects with nine unruptured bifurcation aneurysms were enrolled. Mean aneurysm size was 7.2±1.2 mm (range 5.5–9.7 mm). An adequate aneurysm occlusion (defined as a complete occlusion or a neck remnant) was achieved in 6/9 patients (66.7%) at 6 months and 4/7 patients (57.1%) at 36 months follow-up. Two of the nine subjects experienced a major stroke (22.2%), including one on postoperative day 1 due to a procedure-related parent vessel occlusion and subsequent ischemic stroke. The other major stroke occurred within the 36-month follow-up period during treatment of a separate aneurysm with coils, leading to perforation with hemorrhagic stroke causing a permanent neurological deficit.

Conclusion The ARTISSE ISD was successfully deployed in all nine cases. There were, however, several procedure-related complications and results in terms of angiographic aneurysm occlusion were modest.

INTRODUCTION

The concept of intra-aneurysmal flow disruption (IAFD) has progressively emerged as a new paradigm for the treatment of primarily bifurcation aneurysms, intending to address a broader array of aneurysms with endovascular treatment. IAFD devices have in common to be self-expanding devices that are placed inside the aneurysm cavity, providing a mesh of metal across the neck of the aneurysm that isolates it from the parent artery blood flow to provoke blood stasis and progressive thrombosis of the sac. Two IAFD devices, the WEB (Woven Endobridge, Microvention, Aliso Viejo, California, USA) and the LUNA AES (LUNA Aneurysm Embolization System, Medtronic, Irvine, California, USA) emerged a decade ago, with promising results in animal and human studies. The WEB has been evaluated in several multicenter prospective observational studies in Europe and the USA and is currently the sole commercially available IAFD device. Originally, the LUNA AES had an ovoid shape allowing the device to treat either bifurcation or sidewall aneurysms. The LUNA AES was later redesigned into a new device called the ARTISSE intrasaccular device (ISD) (Medtronic) which exists in two shapes: ovoid and flared to better conform to the various aneurysm anatomies. We report our experience with the very first patients treated with this new device.

METHODS

The study was conducted on a single-center cohort of patients included in a prospective study of aneurysms treated endovascularly (Standardized Long-Term Follow-up of Patients After Endovascular Embolization of a Brain Aneurysm - ANENDO-VASC - NCT02878967) with the ARTISSE ISD. The ethics committee of the Fondation Rothschild Hospital and the French Data Protection Agency approved this research project. Written informed consent was obtained for all subjects.

Study purpose, device indications and participants

Similar to a previous study on the LUNA device, the ARTISSE ISD study is a single-arm, long-term (36-month) follow-up study of the first ever patients treated with the ARTISSE ISD in order to collect safety and efficacy data on this device for the treatment of saccular intracranial aneurysms in accordance with the manufacturer’s instructions for use. The ARTISSE ISD is indicated for the endovascular treatment of saccular intracranial bifurcation and sidewall aneurysms with a height of 5.4–9.6 mm, a width of 4.5–8.0 mm, with no particular threshold regarding the dome-to-neck ratio. Nine subjects at one site were treated with the ARTISSE ISD. The nine patients were screened and selected on an ‘intention-to-treat’ basis. Subject enrollment was initiated in December 2016 and completed in May 2017.

Inclusion and exclusion criteria

Each subject was required to meet all of the following inclusion criteria: age 18–75 years;
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diagnosed with an intracranial aneurysm matching the manufacturer’s instructions for use for the ARTISSE ISD; no previous treatment (endovascular or surgical) of the aneurysm. Exclusion criteria included any of the following conditions: the subject had a fusiform aneurysm; the target aneurysm had been previously treated by surgical or endovascular means; the presence of congestive heart failure, cardiac arrhythmia, unstable coronary artery disease, respiratory disease, cancer or symptomatic infection; the subject had a history of drug use, alcoholism, or neurovascular or neurological disease; the use of contrast media or angiography was contraindicated for use in the subject; the subject had participated in a clinical drug trial within the previous 28 days; the subject was simultaneously using steroid or immunosuppressive therapy; and the subject had a comorbid disease or condition that was expected to compromise his or her ability to complete follow-up assessments.

The ARTISSE device

The ARTISSE ISD is a CE marked self-expandable spheroid or flared implant made from a double layer of 72 nitinol radiopaque wires. Available sizes for the device are 4.5–8.5 mm. It is a refinement of the LUNA AES, with several adjustments made to overcome some technical limitations of its predecessor. The LUNA AES required a 0.027 inch microcatheter for delivery, and its cage had limited visibility under fluoroscopy. The ARTISSE device requires a smaller profile 0.021 inch microcatheter for delivery, and the engineering of its wires has been modified in order to improve visibility.

Treatment planning

Initial training with the device was organized for the operators. Three-dimensional silicone models of the first three patients identified for this study were printed from the patient’s three-dimensional rotational angiographies obtained on previous cerebral angiograms. The models were brought to the angiosuite and all three procedures were rehearsed in order to test several device sizes and get used to the deployment of the ARTISSE ISD.

Treatment

All procedures were performed via femoral approach, under general anesthesia and full anticoagulation with heparin (with a targeted activated clotting time 2–3 times above the patient’s basic value). Patients also received an intravenous bolus of aspirin (250 mg) at the beginning of the procedure. Procedures were conducted with 6-French guiding catheters and an intermediate catheter. Microcatheters (with an internal lumen of 0.021 inches) for device delivery included Prowler Select Plus (Codman, Raynman, Massachusetts, USA) and Phenom 21 (Medtronic).

Data collection, postoperative follow-up schedule and antiplatelet therapy

The following data were prospectively collected for each patient: demographic information; aneurysm information (location, size and neck size); and procedure information including date, size of device used, access catheters used, perioperative medications, occurrence of complications, and use of additional devices during the procedure. A modified Rankin Scale (mRS) score was collected for each subject before treatment and at discharge, and at 6-month and 36-month follow-ups. Management of post-procedural antiplatelet therapy was left to the physician’s discretion. Angiographic assessment was completed by a single operator for each follow-up.

Safety analysis

Adverse events were categorized using previously specified definitions of neurological events of interest: major stroke (ie, a stroke leading to permanent disability), minor stroke (ie, a stroke that would cause permanent symptoms with no disability), transient ischemic attack, intracranial hemorrhage and retreatments.8 Disability was assessed using the mRS. Morbidity was defined as mRS >2 if baseline mRS was ≤2, an increase in mRS of 1 or more if baseline mRS was >2, or mRS >2 if aneurysm was ruptured at baseline. All adverse events were reviewed and adjudicated by the same operator.

Efficacy analysis

The efficacy variables were related to the ability of the device to occlude the intracranial aneurysm at various time points. Specific variables evaluated in this study included the angiographic assessment of aneurysm occlusion grade according to the Raymond–Roy classification scale, parent vessel compromise, and occlusion durability. Occlusion grade and parent vessel compromise were assessed by the operator on the procedural baseline and 6-month and 36-month follow-up digital subtraction angiogram (DSA). Angiographic data were available immediately after the procedure and at 6-month and 36-month follow-ups for nine, nine and seven patients, respectively.

Follow-up schedule

The patients were followed up at 6 and 36 months with a clinical assessment (including an extended neurological assessment) and a cerebral DSA.

Statistical methods

Nine eligible subjects were enrolled after informed consent was obtained, with the intent of having at least seven evaluable subjects after accounting for a 20% dropout rate. Continuous variables are presented as mean±SD and categorical variables are shown as frequency (n) and percentage (%). Because this was a post-market study focused exclusively on safety and efficacy, no control group was enrolled.

RESULTS

Subject demographics and medical history

Nine subjects (all women) with nine aneurysms were enrolled for treatment in this study. Subject enrollment occurred between December 12, 2016 and May 2, 2017. The mean±SD age was 58.8±9.6 years (table 1). Two subjects had a first-degree family history of aneurysms (one ruptured, one unruptured).

Aneurysm characteristics

At baseline, all nine aneurysms were unruptured. All aneurysms were either bifurcation or terminal aneurysms and measured 5–10 mm. The mean dome-to-neck ratio was 1.82:1 (table 1).

Procedural data

Nine ARTISSE ISD devices were implanted in nine aneurysms: eight were delivered at the first attempt (88.9%) and one was deployed at the second attempt (11.1%) after changing the size of the ARTISSE ISD. There were two (22.2%) thrombolic procedural complications.

Procedural complication 1

One case of bifurcation aneurysm required the emergency bail-out deployment of two stents in Y-configuration due to acute parent vessel occlusion immediately after deployment of
The ARTISSE ISD. The patient received a 20 mg bolus of abciximab followed by continuous infusion. At postoperative day 1, abciximab was discontinued and the patient was prescribed dual antiplatelet therapy for 3 months (aspirin 250 mg daily) then aspirin 250 mg daily for a further 3 months. The patient was completely asymptomatic from that complication (mRS=0).

Procedural complication 2

Another patient developed an acute ischemic stroke at postoperative day 1 because of a parent vessel occlusion and was immediately brought to the angiographic suite for recanalization which was unsuccessful. The patient had a major stroke with permanent disability (mRS=3).

Device effectiveness

Post-procedural angiographic evaluation was performed for all nine ARTISSE ISD-treated aneurysms; 6-month angiographic follow-up data were evaluated in nine aneurysms and 36-month angiographic follow-up data in seven aneurysms (table 2).

Immediately after ARTISSE ISD implantation, complete occlusion was observed in 3/9 aneurysms (33.3%) and residual aneurysm was observed in 6/9 aneurysms (66.6%). At 6-month follow-up, complete occlusion was obtained in 3/9 aneurysms (33.3%), neck remnant in 3/9 aneurysms (33.3%), and residual aneurysm in 3/9 (33.3%). At 36-month follow-up, complete occlusion was achieved in 2/7 aneurysms (28.6%), a neck remnant was visible in 2/7 aneurysms (28.6%), and a residual aneurysm in 3/7 patients (42.8%).

No ARTISSE ISD-treated aneurysm bled during the follow-up period. One patient (11.1%) required retreatment at 6 months after the follow-up DSA showed complete recanalization due to retraction of the ARTISSE ISD into the sac (figure 1).

One subject underwent endovascular treatment of a second untreated aneurysm with coiling; the procedure was complicated with aneurysm perforation and subsequent intraventricular hemorrhage with neurological sequelae (mRS=3). No patient died during follow-up.

Antiplatelet therapy during follow-up

Two patients (22.2%) with acute procedural thrombotic complications were put on blood thinners (see above for details). The first patient was put on aspirin and ticagrelor following a bail-out Y-stenting during ARTISSE ISD implantation. The second patient was put on aspirin following an ischemic stroke on postoperative day 1 because of parent vessel occlusion by the ARTISSE ISD. The other seven patients did not take any blood thinners following the procedure.

DISCUSSION

This series represents the first cohort of subjects treated with the ARTISSE ISD. The device was successfully deployed in all nine cases. The mid-term (6 months) and long-term (36 months) angiographic follow-up results were modest (3/9 (33.3%) residual aneurysms at 6 months and 3/7 (43%) residual aneurysms at 36 months), especially for aneurysms ≥7 mm. Moreover, (sub-)acute thrombotic events occurred in two of the nine patients (22.2%): one acute per-procedural parent vessel occlusion which required bail-out Y-stenting with no clinical consequence for the patient; and one branch occlusion on postoperative day 1 which led to a major stroke despite an urgent endovascular recanalization procedure.

Comparison between ARTISSE ISD and the LUNA AES

The ARTISSE ISD is an evolution of the former LUNA AES in order to address aneurysms with a height of 5.4–9.6 mm, a width
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of 4.5–8.0 mm using a smaller profile microcatheter (0.021 inch for the ARTISSE ISD vs 0.027 inch for the LUNA AES). The LUNA AES was indicated for endovascular embolization of a broader spectrum of saccular intracranial aneurysms with a height of 4.7–12.6 mm and a width of 3.0–8.5 mm. The need for a 0.027 inch catheter for the LUNA AES was a technical obstacle for some operators/cases, which encouraged the development of a system compatible with a smaller profile microcatheter. The detachment system of the LUNA AES was mechanical, unlike the ARTISSE ISD which has an electrolytical detachment system. Another limitation of the LUNA AES was lack of visibility of the cage itself, which pushed the operator to refer to the proximal and distal radio-opaque markers for device positioning. Engineers have tried to overcome this limitation by modifying the manufacturing process. While the LUNA AES was made of 0.0011 inch (27.9 μm) pure nitinol wires, the ARTISSE ISD is made of thinner (0.00095 inch (24.1 μm)) drawn filled tubing (nitinol +15% platinum composite) wires. While this may have increased device visibility, it might also have impacted the elastic properties of the ARTISSE ISD which was frequently prone to shape modification in our series (figure 1). This might explain, at least in part, our relatively modest results in terms of angiographic occlusion. Immediate angiographic occlusion was rarely observed in our experience (3/9 aneurysms (33.3%)), even though the patients had only received a bolus of aspirin for the procedure. A previous multicenter study with the LUNA AES reported immediate angiographic occlusion of the aneurysm in only 11/63 aneurysms (18%). The absence of immediate angiographic occlusion is thought to be one of the factors that predict treatment failure or aneurysm recurrence at follow-up in patients treated with IAFD. At 6 months follow-up, the ARTISSE ISD led to adequate aneurysm occlusion (ie, complete occlusion or neck remnant) in 6/9 aneurysms (66.7%), while the same study with the LUNA AES showed an adequate occlusion at 6 months in 46/59 aneurysms (78.0%). More importantly, the performance of ARTISSE ISD was not improved over time, with an adequate occlusion of only 4/7 aneurysms (57.1%) at 3-year follow-up, while the LUNA AES had rates of 79.2% (42/53 aneurysms) at the same timepoint. Our results with the ARTISSE ISD are inferior to angiographic results usually obtained with coiling. Our sample size with the ARTISSE ISD is much smaller and comparisons with other devices should thus be made with a lot of caution, but our early results seem to indicate that the refinements that led to the ARTISSE ISD might have negatively impacted its performance. The manufacturer is aware of the results of this study and informed us that they are working on a new version of the ARTISSE.

Limitations

Our results suffer from all the inherent limitations of a single-center observational study. The study sample is small and our rates of safety and efficacy endpoints should thus be interpreted with caution. There was no core laboratory for the external adjudication of our angiographic outcomes,
which usually leads to some discrepancies compared with self-adjudication.\textsuperscript{13} There might be a learning curve with the device as with any similar intrasaccular flow diverter\textsuperscript{14,15} and results might improve with time and experience.\textsuperscript{16} However, our unexpectedly high rates of procedural thromboembolic events and long-term angiographic residual aneurysms are still relevant for colleagues who might want to try this new device.

**CONCLUSION**
The ARTISSE ISD showed excellent radiopacity during deployment and positioning, however rates of procedural thromboembolic events were high and angiographic results in terms of aneurysm occlusion were modest. A device shape modification was frequently observed at follow-up and might be explained by the device manufacturing modification.

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