Reconstructive endovascular treatment of intracranial aneurysms with the Willis covered stent: medium-term clinical and angiographic follow-up

Clinical article

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Object. Placement of covered stents has emerged as a promising therapeutic option for cerebrovascular diseases. However, the medium- and long-term efficacy and safety of covered stents in the treatment of these diseases remain unclear. The purpose of this study was to evaluate the medium-term clinical and angiographic outcomes of covered stent placement for the treatment of intracranial aneurysms.

Methods. The authors’ institutional review board approved the study. Thirty-four patients (13 females and 21 males; mean age 41.9 years) with 38 intracranial aneurysms were treated with the Willis covered stent. Clinical and angiographic follow-up were performed at 3 months, at 6–12 months, and annually thereafter. The initial procedural and follow-up outcomes were collected and analyzed retrospectively.

Results. Forty-two covered stents were successfully implanted into the target artery in 33 patients with 37 aneurysms, and 1 covered stent navigation failed in 1 patient. A complete aneurysm exclusion was initially achieved in 24 patients with 28 aneurysms, and a minor endoleak occurred in 9 patients with 9 aneurysms. Postoperatively, 2 patients died of complications related to the procedure. Angiographic and clinical follow-up data are available in 30 patients. The angiographic follow-up (17.5 ± 9.4 months [mean ± SD]) exhibited complete occlusion in 28 patients with 31 aneurysms, and incomplete occlusion in 2 aneurysms, with an asymptomatic in-stent stenosis in 3 patients (10%). The clinical follow-up (26.7 ± 13 months [mean ± SD]) demonstrated that 16 patients (53.3%) experienced a full recovery, and 14 patients (46.7%) improved. No aneurysm rupture, thromboembolic events, or neurological deficits resulting from closure of a perforating vessel by covered stent placement occurred.

Conclusions. Endovascular reconstruction with the Willis covered stent represents a safe, durable, and curative treatment option for selected intracranial aneurysms, yielding an excellent medium-term patency of the parent artery and excellent clinical outcomes. (DOI: 10.3171/2010.9.JNS10373)

KEY WORDS • covered stent • endovascular procedure • intracranial aneurysm • in-stent stenosis

Covered stent placement has emerged as a promising therapeutic alternative to the established neurosurgical or endovascular techniques for the treatment of cerebrovascular diseases, including intractable and complicated intracranial aneurysm, carotid-cavernous fistula, CA stenosis, and CA blowout. The reported immediate and medium-term follow-up results suggest that covered stent placement is a safe and effective method in select cases. However, the medium- and long-term efficacy and safety of covered stents in the treatment of these diseases remain unclear due to the lack of a large patient sample and longer-term follow-up. Although the longest reported clinical and angiographic follow-up has been more than 2 years, the number of patients remains low. On medium- and long-term follow-up, sufficient evidence about the efficacy and safety of covered stents has not been provided. Concerns about covered stent placement for the treatment of intracranial neurovascular diseases remain.

In this study, the medium-term clinical and angiographic follow-up outcomes of patients who had undergone covered stent placement for the treatment of intracranial aneurysm were reported. To our knowledge, this study is the largest series reported on the medium-term clinical and angiographic outcomes of covered stent placement for the treatment of intracranial aneurysm.
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Methods

Patient Population

Between April 2005 and May 2009, 34 patients with 38 intracranial aneurysms (4 patients each harbored 2 aneurysms) were treated with the Willis covered stent (Micro-Port). Clinical and preliminary radiological data have been reported previously in 28 of these patients. Of the 34 patients, 21 were male and 13 were female, and they ranged from 11 to 64 years of age (41.9 ± 11.9 years [mean ± SD]). At presentation, 10 patients had SAH and 24 had no SAH. Of the 10 patients with SAH, 9 had Hunt and Hess Grade II lesions, and 1 had Grade III SAH. Of those without SAH, 2 patients with incidental aneurysms were asymptomatic; 13 displayed mass effects, including loss of visual acuity, diplopia, cranial nerve palsies, and/or hemiparesis; 6 had proptosis either associated with or not associated with conjunctival injection; and 3 had epistaxis either associated with or not associated with visual loss or blindness.

Of the 38 aneurysms, 22 were large (10–25 mm) or giant (> 25 mm), and 16 were small (< 10 mm); 16 were pseudoaneurysms, 21 were saccular aneurysms, and 1 was a recurrent fusiform dissecting aneurysm that occurred after balloon-in-stent assisted coil insertion. Of the 16 pseudoaneurysms, 9 were traumatic and 7 were complicated by embolization of the carotid-cavernous fistula with an endovascular detachable balloon. Two of the 21 saccular aneurysms were recurrent after coil insertion. Twenty-seven of the aneurysms were wide necked (≥ 4 mm or fundus/neck ratio ≤ 2), and 11 were small necked (< 4 mm or fundus/neck ratio > 2). Thirty-seven aneurysms were located in the cranial ICA and 1 was in the VA. The aneurysms were located in the C1 (2 lesions), C3 (1), C4 (11), C5 (4), C6 (5), C7 (14), or V1 (1) segments according to the Bouthillier classification.

This study was approved by our institutional review board committee, and all patients or the patient's family gave their written informed consent.

The Willis Covered Stent

The Willis covered stent is a balloon-expandable endoprosthesis composed of a bare stent and an expandable polytetrafluoroethylene membrane. Its structure has been previously described in detail. The bare stent is sculpted by laser from a piece of high-grade cobalt chromium super alloy tube with a thickness of 0.06 mm. The expandable polytetrafluoroethylene membrane with a thickness of 30–50 µm was glued along the length of the stent struts. The delivery system is a rapid-exchange balloon system with a working length of 145 cm. At present, Willis covered stents with diameters of 3.5, 4.0, 4.5, or 5.0 mm and lengths of 7, 10, 13, 16, or 19 mm are available.

Endovascular Procedure

Patients were treated after induction of general anesthesia by using the previously described techniques of covered stent placement. A 6 Fr Envoy guiding catheter (Cordis Endovascular) was initially positioned in the diseased ipsilateral ICA or VA, and a microguidewire of 300- or 205-cm length and 0.014-in diameter (Transend floppy or platinum wire, Boston Scientific) was navigated into a distal branch of the MCA or the PCA. The Willis covered stent used initially in each patient had a diameter ≥ 0.5 mm larger than that of the parent artery and a length ≥ 4 mm longer than the aneurysm neck. Using roadmap guidance, the stent was navigated over the microguidewire and bridged the aneurysm orifice. Multiple control angiograms were obtained to confirm the positioning and to avoid covering any important side branch, such as the AChA or PICA. The Willis covered stent was then deployed with 5 atm pressure.

Angiography was performed immediately after deflation of the balloon to confirm correct placement of the stent and satisfactory occlusion of the aneurysm. If an endoleak was observed, reinflation of the proximal or distal of the grafts was performed with 5–6 atm pressure to ensure maximum expansion of the stent, thereby improving its apposition and eliminating the endoleak. If an evident endoleak persisted, another covered stent that had the same diameter as the first one and a length as short as possible was used to cover the orifice of the endoleak adjacent to the first covered stent. Both covered stents overlap each other at least 3 mm. Angiography was again performed immediately after this procedure, and a head CT scan was obtained for evaluation of possible complications.

The procedure was performed after therapeutic heparinization had been administered, with activated clotting time of approximately 300 seconds. The patients received heparin for at least 72 hours after the procedure. Generally, patients were pretreated with 100 mg aspirin and 75 mg clopidogrel daily for 3 days before the procedure. If covered stent placement was performed urgently, a loading dose of 300 mg clopidogrel and 300 mg aspirin were administered through the nasogastric tube before the procedure. Postprocedure, the patients were instructed to continue the dual antiplatelet regimen for at least 6 months, and to take aspirin alone thereafter.

Follow-Up and Postoperative Outcome Evaluation

After the procedure, follow-up angiography and head CT scanning was performed at 3 months, at 6–12 months, and annually thereafter. Clinical follow-up to determine cranial nerve deficits, any adverse events, and any change from baseline neurological status related to the devices or the procedure was performed at discharge and at every admission for follow-up angiography or every visit to the outpatient clinic. Data on initial and final radiological results and clinical outcomes were retrospectively collected and analyzed by 2 authors (H. Q. T. and Y. D. L.; by consensus). The angiographic data were categorized into the categories of complete occlusion, no residual cavity, and no endoleak; or incomplete occlusion, a residual cavity, or an endoleak. The in-stent stenoses were categorized as normal, mild stenosis (≤ 29%), moderate stenosis (30%–69%), severe stenosis (70%–99%), or occlusion (> 99%–...
were graded into 4 types: 1) a full recovery from the neurological symptoms that existed before treatment, 2) improved neurological symptoms; 3) unchanged symptoms; or 4) a deterioration (also referred to as aggravation) of the neurological symptoms, as described previously.

Results

Postprocedural Angiographic Results

A total of 42 covered artery stents were successfully implanted into the target artery in 33 patients with 37 aneurysms, and 1 covered stent navigation failed in 1 patient with 1 aneurysm. Two tandem aneurysms in 2 patients were treated with a single stent, 28 aneurysms each were treated with a single stent, 3 aneurysms each were treated with 2 stents, and 2 aneurysms each were treated with 3 stents. The number of covered stents placed per aneurysm was 1.1 ± 0.6 (mean ± SD). Complete aneurysm exclusion was achieved in 24 patients with 28 aneurysms (28 of 37 aneurysms; 75.7%) immediately after the procedure, whereas a minimal endoleak persisted in 9 patients with 9 aneurysms. All patients, except 1 in whom an in-stent acute mural thrombosis occurred immediately after the procedure, showed excellent patency of the parent artery immediately after the procedure. In 2 patients with C5 traumatic aneurysms, the closure of the OphA by covered stent placement was observed, and no acute visual acuity decrease was noted after the procedure. In the remaining 31 patients, no substantial side branches or perforating arteries, such as the PCoA, OphA, AChA, or PICA, were occluded by the stent.

Procedural Complications

There were no adverse events related to the navigation of the covered stent in any of the patients. The delivery of the Willis covered stent was successful, without migration and collapse of the covered stent, in 33 patients. During the treatment, lethal complications related to the procedure occurred in 2 patients. In 1 patient in whom complete exclusion was achieved, an in-stent acute mural thrombosis occurred immediately after the procedure. This patient was treated without anticoagulation and antiplatelet therapy because of an acute SAH, and therefore experienced a large area of cerebral infarction and finally died 22 days after the procedure. In the other patient in whom a minimal endoleak persisted, a severe SAH occurred due to the laceration of perforating vessel originating from the parent artery, resulting from balloon re-inflation; this patient finally died within 1 month after the procedure. In the remaining 32 patients, no morbidity or death occurred during or after the procedure.

Follow-up Angiographic Outcomes

After the procedure, 1 patient in whom 2 tandem aneurysms were excluded completely was lost to follow-up after discharge. In the remaining 30 surviving patients, follow-up angiography studies ranging from 3 to 28 months (17.5 ± 9.4 months [mean ± SD]) were available. In 22 patients with 25 aneurysms with initial complete occlusion (except in 1 patient harboring 1 aneurysm in which a delayed minimal endoleak was observed at the 3-month follow-up), complete occlusion of the aneurysm was still observed with reconstruction of the parent artery (Fig. 1). In 8 patients with initial minimal endoleak, no further treatment was required, and the spontaneous resolution of minimal endoleak was observed in 7 patients at an average of 4.7 months (range 3–7 months); in the remaining patient a persistent minimal endoleak was found at the 11-month follow-up, but an obvious shrinkage of the aneurysm cavity was noted. In 1 patient with a delayed minimal endoleak at the 3-month follow-up, the persistent minimal endoleak remained at the 10-month follow-up, but the residual aneurysm cavity showed an obvious shrinkage compared with follow-up angiography at 3 months. None of the patients, including those with or without a residual minimal endoleak, experienced aneurysm rupture during the observation period.

Three of 30 patients (10%) with angiographic follow-up had angiographic evidence of in-stent stenosis at long-term follow-up. Two patients had approximately 60% stenosis at 6 months (Fig. 2); they did not comply with our prescribed dual antiplatelet regimen within 6 months after discharge. Another patient had ≤ 30% stenosis at 6 months. This individual was previously treated with balloon-in-stent assisted coil occlusion and had a history of hypertension and evident arteriosclerosis of the VA. During the entire observation period, the degree of in-stent stenosis remained stable, and no progressive aggravation or resolution of this condition was observed. None of these patients were symptomatic, and did not require treatment for the stenosis.

The studies obtained at the final angiographic follow-up demonstrated that complete occlusion was achieved in 28 patients with 31 aneurysms (31 of 33 aneurysms; 93.9%), and incomplete occlusion was achieved in 2 patients with 2 aneurysms. In 3 (10%) of 30 patients with 3 (9%) of 33 aneurysms, there was an asymptomatic mild-to-moderate in-stent stenosis.

Follow-Up Clinical Outcomes

The clinical follow-up results were available in 30 patients, with a range of 3 to 48 months (26.7 ± 13 months [mean ± SD]). At the final clinical follow-up evaluation, 16 patients (53.3%) experienced a full recovery, and 14 (46.7%) improved. The neurological symptoms that existed before treatment did not worsen in any of the patients. No delayed thromboembolic or ischemic events in the stent-grafted vascular territories and no bleeding events were reported by any of the patients, including those in whom the case was complicated with in-stent stenosis or in whom there was a residual minimal endoleak, and all of these 30 patients were alive at the time of this report. In 2 patients with closure of the OphA by covered stent placement, no delayed visual acuity decrease or loss and no visual field deficit were noted.

Discussion

The most important findings in the present study are
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the following: 1) endovascular reconstruction with the Willis covered stent for the treatment of selected intracranial aneurysms has a higher rate of complete occlusion and favorable durability; and 2) the long-term patency of covered stents in intracranial aneurysm treatment was excellent, with a low rate of in-stent stenosis.

**Therapeutic Efficacy of Intracranial Aneurysm Occlusion With the Willis Covered Stent**

Endovascular endosaccular coil occlusion has emerged as an accepted and, in some cases, preferred treatment for cerebral aneurysms. However, the technique has the major shortcomings of incomplete treatment and questionable long-term durability. Raymond et al. reported a 38.3% rate of complete angiographic occlusion at the 12-month follow-up evaluation in a series of 353 consecutive coil-treated aneurysms. Kole et al. reported a 19% rate of complete occlusion in a series of 131 coil-treated aneurysms with long-term angiographic follow-up (mean 18 months). In the International Subarachnoid Aneurysm Trial, a 66% rate of complete angiographically confirmed occlusion was observed in a cohort largely (91%) composed of small aneurysms. These rates of occlusion are even lower in selected subgroups such as large, giant, wide-necked, and nonsaccular aneurysms. In the present series, initial complete aneurysm occlusion was achieved in 75.7% of the lesions, and final complete aneurysm occlusion was achieved in 93.9% of the lesions at the final follow-up of this report. No treated lesions, except 1 aneurysm in which a delayed minimal endoleak was observed at the 3-month follow-up, demonstrated refilling during an average of 17.5 months of follow-up. Moreover, no bleeding events were reported by any of the patients. Compared with the efficacy of endosaccular coil insertion, our results for either initial or final complete aneurysm occlusion had a favorable comparability. When considering the types of lesions composing the present series—large, giant, wide-necked, and nonsaccular aneurysms, and aneurysms for which previous treatment had failed, this level of efficacy is even more remarkable.

**Fig. 1.** Neuroimages obtained in a 60-year-old man suffering from ptosis of left eye for 3 days. **A:** Anteroposterior cerebral angiography shows a giant aneurysm on the left C5 segment of the ICA. **B:** The road mapping performed during the procedure shows the expanded covered stent at the level of the aneurysm orifice of the parent artery (arrows). **C:** Anteroposterior cerebral angiography study obtained immediately after the procedure shows a minimal endoleak into the aneurysm (arrow). **D:** Follow-up cerebral angiography study obtained 14 months after the procedure shows complete exclusion of the aneurysm, with excellent patency of the parent artery.

**Fig. 2.** Neuroimages obtained in a 58-year-old man suffering from head distention and dizziness for 1 month. **A:** Left lateral cerebral angiography study shows an aneurysm (arrow) adjacent to the PCoA on the left C7 segment of ICA. **B:** The road mapping performed during the procedure shows the expanded covered stent (arrows) at the level of the aneurysm orifice of the parent artery. **C:** Left lateral cerebral angiography study obtained immediately after the procedure shows complete exclusion of the aneurysm, with reconstruction of the parent artery. **D:** Follow-up cerebral angiography study obtained 23 months after the procedure shows complete disappearance of the aneurysm, with an asymptomatic stenosis (arrow) of the parent artery.
In-Stent Stenosis

In-stent stenosis is an important concern in covered stent placement for the treatment of intracranial neurovascular diseases. The in-stent stenosis rate associated with the use of covered stents in coronary circulation has been reported to be approximately 30%. However, in our series, 3 patients (10%) with angiographic follow-up presented with an asymptomatic in-stent stenosis at an average of 17.5 months, results that are similar to those reported by Saatci et al. and to our previously reported findings, and far less than the rate associated with the use of covered stents in the coronary circulation. We presumed that different underlying characteristics of the vascular wall in aneurysms and in coronary atherosclerosis may account for differences in the rates of in-stent stenosis. In the present study, the patients were relatively young, with a mean age of 41.9 years, and the majority of presentations were due to trauma. These patients had fewer risk factors of hypertension or atherosclerosis compared with patients in whom covered stents were used in the coronary circulation. Additionally, the Willis covered stent was delivered at a nominal pressure of 5 atm, which is far less than that of coronary balloon-mounted stents (14 atm). The lower delivery pressure resulted in less endothelial injury, which has been demonstrated to be closely related to neointimal growth and the incidence of in-stent stenosis. Most importantly, all except 2 patients strictly complied with our prescribed dual antiplatelet regimen within 6 months after discharge; thus, platelet aggregation was effectively prevented and the process of intimal hyperplasia was reduced.

In-Stent Thrombosis and Thromboembolic Events

Possible in-stent thrombosis and thromboembolic events are another important concern in covered stent placement for the treatment of intracranial neurovascular diseases. A number of variables correlate with a higher probability of in-stent thrombosis, including small vessel size, proximal or distal dissection, and underdilation or thrombogenicity of the stent. A review of the literature revealed only 3 reported patients in whom the parent vessel was asymptotically occluded on follow-up cerebral angiography. In 1 patient, occlusion of the ICA was found 1 week after stent placement for a posttraumatic petroclinoid ICA pseudoaneurysm. This patient also had a distal MCA pseudoaneurysm; thus, minimal anticoagulation was used (daily aspirin). In the other 2 cases, ICA occlusion was found at the 1-month angiographic follow-up, and was thought to be the result of discontinuation of the antiplatelet therapy. In the present study, all patients were pretreated with oral aspirin and clopidogrel and underwent systematic heparinization during the procedure; then low-molecular-weight heparin was given subcutaneously for 72 hours, followed by oral aspirin and clopidogrel, and no acute or delayed in-stent thrombosis and thromboembolic events occurred during and after the procedure, except that an in-stent acute mural thrombosis occurred in 1 patient immediately after the procedure. This favorable result was attributed to a combination treatment with ticlopidine/clopidogrel and aspirin, which have been demonstrated to reduce the risk of in-stent thrombosis significantly. However, the optimal treatment regimen has yet to be determined.

Judicious Coverage of Regional Perforating Vessels

Covered stents by definition have the pitfall of occluding small perforating vessels in the region in which the stent has been placed. Therefore, concern also exists regarding occlusion of the ostia of small side branches and perforating arteries with stent placement, which may result in ischemia or infarction. Although the use of covered stents in the ICA below the level of the AChA and PCoA, in the distal VA, in the extradural VA, or in any location that is free of side branches or perforating arteries is well tolerated by patients, as documented in the literatures, the existing data are too few to make a definitive statement about the safety of this practice. In the present study, the treatment resulted in occlusion of the OphA origin in 2 patients; no acute or delayed visual dysfunction was observed during follow-up. It is likely that reconstruction of the OphA from the ECA collateral vessels by means of branches of the OphA occurred. Although the closure of the OphA was uneventful in the present study, caution should be taken because occlusion of the OphA is associated with permanent blindness in 10% of cases. Preoperative temporary balloon occlusion of the OphA and ICA may be attainable to evaluate the adequacy of collateral flow and prevent possible impairment of vision. Additionally, extreme caution should be taken not to cover the AChA, the fetal-type PCoA, or the PICA origin when the covered stent is placed in the distal ICA or the distal VA, from which an eloquent perforating vessel originates. In our series, closure of the AChAs or PICAs was successfully avoided due to an appropriate case selection and careful review of the location of the perforating arteries, or to improvement in angiographic techniques, and no postprocedural neurological deficits were observed.

Our study has some limitations. First, although the current series is the largest reported to date, the number of patients treated remains small and the duration of follow-up remains short; furthermore, in some cases only 3-month follow-up was completed; thus, expanded clinical trials are required to determine the long-term outcomes. Second, the current patients are highly selected. The patients with a distance of < 2 mm between the aneurysm orifice and the AChA, fetal-type PCoA or PICA, or an extremely tortuous parent artery that prohibited navigation and placement of the Willis covered stent delivery system were excluded. Therefore, this selection bias results in a higher technical success rate and lower complication rate. Third, the present study lacked a comparison group receiving other treatment, such as coil insertion or stent-assisted coil placement; consequently, the proposition that the efficacy and safety of the Willis covered stent for the treatment of intracranial aneurysms are superior to those with the currently recommended approach of coil embolization remains unproved.

Conclusions

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Willis covered stent is an attractive therapeutic option for intractable and complex intracranial aneurysms in selected patients. This treatment modality has a higher rate of complete occlusion and favorable durability. An excellent medium-term patency of parent artery and clinical outcomes can be achieved.

Disclosure

This study was supported by the National Natural Scientific Fund of China (30570540), the Shanghai Important Subject Fund of Medicine (05 IV 023 and 074119505), and the Program for Shanghai Outstanding Medical Academic Leader (LI 0616). The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: MH Li, Tan, YD Li, JB Wang. Acquisition of data: MH Li, Tan, Zhang, Zhu, W Wang. Analysis and interpretation of data: MH Li, Tan, YD Li, JB Wang, Zhu, W Wang. Drafting the article: MH Li, Tan. Critically revising the article: MH Li, Tan, YD Li, JB Wang, Zhu. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: MH Li, Tan, YD Li. Study supervision: MH Li.

Acknowledgments

The authors thank Dr. Chun Fang and Jue Wang for their assistance with data collection.

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Manuscript submitted March 11, 2010. Accepted September 15, 2010. Please include this information when citing this paper: published online October 22, 2010; DOI: 10.3171/2010.9.JNS10373.

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