Stent-Assisted Coiling of Intracranial Aneurysms
Predictors of Complications, Recanalization, and Outcome in 508 Cases

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Background and Purpose—Self-expanding stents are increasingly used for treatment of complex intracranial aneurysms. We assess the safety and the efficacy of intracranial stenting and determine predictors of treatment outcomes.

Methods—A total of 508 patients with 552 aneurysms were treated with Neuroform and Enterprise stents between 2006 and 2011 at our institution. A multivariate analysis was conducted to identify predictors of complications, recanalization, and outcome.

Results—Of 508 patients, 461 (91%) were treated electively and 47 (9%) in the setting of subarachnoid hemorrhage. Complications occurred in 6.8% of patients. In multivariate analysis, subarachnoid hemorrhage, delivery of coils before stent placement, and carotid terminus/middle cerebral artery aneurysm locations were independent predictors of procedural complications. Angiographic follow-up was available for 87% of patients at a mean of 26 months. The rates of recanalization and retreatment were, respectively, 12% and 6.4%. Older age, previously coiled aneurysms, larger aneurysms, incompletely occluded aneurysms, Neuroform stent, and aneurysm location were predictors of recanalization. Favorable outcomes were seen in 99% of elective patients and 51% of subarachnoid hemorrhage patients. Patient age, ruptured aneurysms, and procedural complications were predictors of outcome.

Conclusions—Stent-assisted coiling of intracranial aneurysms is safe, effective, and provides durable aneurysm closure. Higher complication rates and worse outcomes are associated with treatment of ruptured aneurysms. Stent delivery before coil deployment reduces the risk of procedural complications. Staging the procedure may not improve procedural safety. Closed-cell stents are associated with significantly lower recanalization rates.

Key Words: aneurysm ■ coil ■ complications ■ recanalization ■ stent

Endovascular therapy is a well-established treatment modality for intracranial aneurysms. Large, complex, wide-necked, and fusiform aneurysms were initially considered unamenable to endovascular coil embolization. With the advent of stents designed specifically for the intracranial circulation, such aneurysms can now be safely and efficiently managed endovascularly.1 Self-expanding stents allow denser aneurysm packing with increased neck coverage and may also improve treatment durability through a combination of flow diversion, parent vessel straightening, and fibroelastic tissue formation along the neck of the aneurysm.2,3 The US Food and Drug Administration approved the Neuroform stent (Stryker Neurovascular, Fremont, California) in 2002, followed by the Enterprise stent (Cordis Neurovascular, Miami, Florida) in 2007, for use in coil embolization of wide-necked intracranial aneurysms. The results of stent-assisted coiling (SAC) have varied widely across different studies. In a French series of 216 aneurysms treated with stents, the rates of permanent morbidity and mortality were as high as 7.4% and 4.6%, respectively. Elsewhere, morbidity and mortality rates with SAC were found to be low.4–7 Several questions remain unanswered: Does the type of stent (open versus closed-cell design) affect the rates of complication and recanalization? Should stents or coils be delivered first? Does staging the procedure provide any benefit for procedural complications or patient outcome? Is stenting of acutely ruptured aneurysms associated with higher complication rates and worse outcomes?

We assess the safety and the long-term efficacy of stent-assisted techniques and determine the predictors of complications, initial aneurysm occlusion, recanalization, and immediate outcome in a series of 552 aneurysms treated at our institution.

Materials and Methods

Thomas Jefferson University institutional review board approval was obtained before data collection. We searched our database for all patients, who were treated with Neuroform and Enterprise stents at our institution between January 2006 and October 2010. A total of 508 consecutive patients with 552 aneurysms met the study criteria and constituted our study population. Medical charts and imaging studies were reviewed to determine patient age, sex, size of aneurysm, location...
of aneurysm, Hunt and Hess grade, procedural specifics, procedural morbidity and mortality, immediate and follow-up angiographic results, rate of retreatment, and rate of rehemorrhage. For some patients included in this study, we have previously reported on the incidence and predictors of in-stent stenosis, as well as the safety and efficacy of SAC in basilar tip aneurysms. This report assesses the safety, efficacy, and long-term results of SAC for the entire cohort and determines predictors of outcome.

All procedure-related complications are reported regardless of their clinical significance. Thromboembolic complications were diagnosed intraoperatively on digital subtraction angiography, clinically as new deficits or change in level of consciousness, or on computed tomography/MRI scans (new infarcts) performed in cases of sudden neurological compromise. Ischemic/thromboembolic complications were also recorded through follow-up. Intraprocedural aneurysm rupture, hemorrhagic complications, and dissections were recorded along with the associated morbidity. Radiographic follow-up (digital subtraction angiography or MR) was scheduled at 6 months, 1 year, 2 years, and 5 years after endovascular procedures. Initial and follow-up angiographic images were compared with determine the rate of aneurysm recanalization. Any aneurysm that displayed a decreasing percentage of occlusion on follow-up angiography was considered recurrent regardless of the need for retreatment. Patient outcomes were assessed at a common time point, that is, at discharge using the Glasgow outcome scale (GOS), and classified as follows: I, deceased; II, vegetative state; III, severely disabled; IV, moderately disabled; and V, mildly or not disabled.

All procedures were performed under general anesthesia and continuous electrophysiological monitoring. Patients with unruptured aneurysms in whom the use of a stent was anticipated were pretreated with daily doses of 81 mg of aspirin and 75 mg of clopidogrel for 10 days before the procedure. After femoral access was obtained, an initial 100-U/kg heparin bolus was administered and activated clotting time was maintained at ≥2 times the patient’s baseline throughout the endovascular procedure. All patients were maintained on daily doses of 75 mg of clopidogrel and 81 mg of aspirin for 2 months, followed by 81 mg of aspirin daily indefinitely. For stent-assisted procedures performed in the setting of a subarachnoid hemorrhage, patients were loaded with 600-mg clopidogrel intraprocedurally and a 50-U/kg heparin bolus after deployment of the first coil.

The decision to use SAC was based on the aneurysm morphology, aneurysm–parent vessel relationship, and comorbidities that rendered a patient a poor surgical candidate. The use of self-expanding stents was generally indicated for wide-necked aneurysms (>4 mm) or those with an unfavorable fundus-to-neck ratio (<1.5) and as a rescue when coils prolapsed into the parent vessel. We prefer to use SAC for unruptured aneurysms and balloon-assisted coil embolization in the treatment of ruptured aneurysms in our institution at the operator’s discretion. Aneurysms were embolized with a variety of bare platinum coils at the operator’s discretion. SAC procedures were either staged or performed during a single session at the operator’s discretion. In staged procedures, the stent was placed first across the aneurysm neck and left to endothelialize for 6 to 12 weeks before the patient was brought back for coil embolization. This usually allowed greater stability and lesser movement of the stent during coil deployment. Single-stage SAC was typically performed using the microcatheter jailing technique in which the stent is deployed after the aneurysm is microcatheterized but before coil deployment. The choice between Neuroform and Enterprise stenting was mostly based on operator preference. In tortuous and difficult vascular anatomy, the Enterprise stent was generally preferred because of its improved navigability and ease of deployment. The Y-stent technique was reserved for wide-necked basilar tip aneurysms, carotid terminus aneurysms, or middle cerebral artery aneurysms that included the orifices of the bifurcation vessels or when a single-stent was not sufficient to prevent coil prolapse into the parent vessel. A telescoping stent technique was finally used to treat selected patients with small blister-like aneurysms, dissecting aneurysms, or large/giant aneurysms.

### Statistical Analysis

Data are presented as mean and range for continuous variables, and as frequency for categorical variables. Analysis was carried out using

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**Table. Location of Treated Aneurysms**

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of Aneurysms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid opthalmic</td>
<td>136 (24.6)</td>
</tr>
<tr>
<td>Paracanoid</td>
<td>122 (22)</td>
</tr>
<tr>
<td>Posterior communicating artery</td>
<td>94 (17)</td>
</tr>
<tr>
<td>Basilar artery</td>
<td>83 (15)</td>
</tr>
<tr>
<td>Carotid terminus</td>
<td>42 (7.6)</td>
</tr>
<tr>
<td>Carotid cavernous</td>
<td>27 (4.9)</td>
</tr>
<tr>
<td>Vertebral artery</td>
<td>21 (3.8)</td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td>16 (2.9)</td>
</tr>
<tr>
<td>Anterior cerebral artery</td>
<td>3 (0.5)</td>
</tr>
<tr>
<td>Anterior choroidal artery</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Anterior communicating artery</td>
<td>7 (1.5)</td>
</tr>
<tr>
<td>Total</td>
<td>552</td>
</tr>
</tbody>
</table>
Excluding the 12 patients in whom stent deployment failed, a single-stent was used in 477 aneurysms (Neuroform in 270, Enterprise in 207), 2 stents in 56 aneurysms (2 Neuroform in 19; 2 Enterprise in 24; and 1 of each in 13), and 3 stents in 7 aneurysms (3 Enterprise in 4; 3 Neuroform in 2; and 1 Enterprise, 2 Enterprise in 1). A Y-stent technique was used in 19 aneurysms.

Complications
Immediate procedural complications occurred in 31 patients (6.2%) causing death in 2 (0.4%) and permanent morbidity in 13 (2.6%). Thromboembolic complications occurred in 24 patients (4.6%) including in-stent thrombosis in 6 (1.2%), new symptomatic infarcts in 14 (2.6%), and clinically silent infarcts in 4 (0.8%). Hemorrhagic complications (1.2%) occurred in 6 patients (intraprocedural aneurysm rupture in 5 and hemorrhagic conversion of an infarct after lytics injection for in-stent thrombosis in 1) and accounted for the 2 deaths in the series. Two patients (0.4%) suffered internal carotid artery dissections and underwent carotid stent placement.

Delayed ischemic complications occurred in 3 patients (0.6%) at a mean of 11 months and resulted in permanent morbidity in only 1 patient. Thus, overall complications occurred in 34 patients (6.8%).

Overall complications were noted in 25% of patients with acutely ruptured aneurysms causing death and permanent morbidity in 12.7%. In those treated electively, complications occurred in 4.7% causing death and permanent morbidity in 1.9% (P<0.001). The complication rate was 9.6% for single-stage SAC versus 5% for multistaged SAC (P=0.1), but the difference was because all patients with ruptured aneurysms underwent single-stage SAC. Complications occurred in 16% of patients when coils were delivered first versus 6.3% when stents were delivered first (P<0.001). Patients treated with a single Neuroform stent had a 7.2% complication rate versus 7.5% with an Enterprise stent (P=0.8). There were no complications in patients treated with a telescoping stent technique. The complication rate did not differ significantly among the first 100 patients (9%; 9/100) treated during the study period and those treated later (6.3%, 25/396, P=0.34). Likewise, there was no significant difference in complication rates between the first half (8.5%, 21/248) and the second half of the cohort (5.2%, 13/248, P=0.16). There was also no significant difference in procedural complication rates between operators with >2-year experience (6.7%, 22/330) and those with <2-year experience (7.2%, 12/166, P=0.82) in endovascular aneurysm treatment.

The following factors were tested for as predictors of complications: age, sex, ruptured aneurysm status, aneurysm location, aneurysm size, previous aneurysm treatment, treatment early versus late in the series, type of stent, stenting technique (single-stent, Y-stent, and telescoping stents), staged treatment, and delivery of coils before stent placement. In univariate analysis, predictors of procedural complications were (1) acutely ruptured aneurysms (P<0.001), (2) coil delivery before stent delivery (P<0.001), (3) single-stage SAC (P=0.1), (4) SAC versus telescoping stent technique (P=0.04), and (5) carotid terminus/middle cerebral artery aneurysm locations versus remaining aneurysm locations (P=0.003). These factors were subsequently entered into a multivariate analysis. In multivariate analysis, acutely ruptured aneurysms (odds ratio [OR]=2.8; 95% confidence interval [CI], 1.1–7; P=0.01), delivery of coils before stent placement (OR=5.2; 95% CI, 2–15; P=0.002), and carotid terminus/middle cerebral artery aneurysm locations (OR=3.2; 95% CI, 1.2–8.5; P=0.02) were statistically significant independent predictors of complications.

Angiographic Outcome
Immediate occlusion (≥95%) was achieved in 428 aneurysms (87.5%). The same factors as above (except telescoping stent technique) were tested for as predictors of immediate aneurysm occlusion. In univariate analysis, negative predictors of immediate occlusion were (1) increasing aneurysm size (>10 mm; P=0.001), (2) increasing age (>65 years; P<0.001), (3) staged SAC (P=0.1), and (4) middle cerebral artery/vertebro-basilar/cavernous aneurysm locations versus remaining aneurysm locations (P=0.003). In multivariate analysis, increasing age (OR=0.5; 95% CI, 0.8–0.9; P=0.02), increasing age (OR=0.5; 95% CI, 0.3–0.9; P=0.02), and staged SAC (OR=0.5; 95% CI, 0.3–0.9; P=0.03) were negative predictors of immediate occlusion.

Radiographic follow-up (digital subtraction angiography or MR angiography) was available for 87% (424/489) of stent-coiled aneurysms at a mean of 26±10.1 months. The rates of recanalization and retreatment were, respectively, 12% (51/424) and 6.4% (27/424). Retreatment consisted of recoiling in 22 patients, additional stent placement and coiling in 2 patients, clipping in 1 patient, pipeline embolization device treatment in 1 patient, and Onyx HD 500 embolization in 1 patient. After excluding patients treated with a combination of different stents, recanalization and retreatment rates were, respectively, 14% (32/226) and 8.8% (16/226) with Neuroform stents versus 9.1% (17/186) and 5.4% (10/186) with Enterprise stents (P=0.1, P=0.2). We have previously reported a 2.5% rate of in-stent stenosis in our series.10

The following factors were tested for as predictors of recanalization: age, sex, ruptured aneurysm status, Hunt and Hess grade, aneurysm location, aneurysm size, previous aneurysm treatment, type of stent, stenting technique, staged treatment, procedural complications, delivery of coils before stent placement, immediate aneurysm occlusion, and follow-up time. In univariate analysis, predictors of recanalization were (1) older age (>65 years; P=0.01), (2) previously coiled aneurysms (P=0.02), (3) larger aneurysms (>10 mm; P<0.001), (4) incompletely occluded aneurysms (P=0.003), (5) Neuroform stent (P=0.1), (6) staged treatment (P=0.1), and (7) cavernous/posterior communicating/middle cerebral artery aneurysms/vertebral (P<0.001). In multivariate analysis, older age (OR=1.03; 95% CI, 1.0–1.1; P=0.03), previously coiled aneurysms (OR=3.4; 95% CI, 1.4–8.1; P=0.005), larger aneurysms (OR=1.1; 95% CI, 1.1–1.2; P<0.001), incompletely occluded aneurysms (OR=1.5; 95% CI, 1.1–6; P=0.04), Neuroform stent (OR=0.4; 95% CI, 0.2–1; P=0.05), and cavernous/posterior communicating/middle cerebral artery aneurysms/vertebral locations (OR=2.2; 95% CI, 1.1–6.1; P=0.03) were statistically significant independent predictors of recanalization.
Of the 28 aneurysms treated with a telescoping stent technique, 19 had available angiographic follow-up at a mean time point of 16.7 months. There was an increase or no change in aneurysm size in 8 cases (42%), and some degree of aneurysm involution in 11 (58%) cases. Only 4 (21%) aneurysms were completely obliterated (>95%) at follow-up. Retreatment was undertaken in 3 patients (16%) using the pipeline embolization device.

Clinical Outcome
Of 496 patients, 467 (94%) achieved a favorable outcome (GOS I-V). Specifically, favorable outcomes were seen in 99% (443/449) of elective patients and 51% (24/47) of subarachnoid hemorrhage patients (P<0.001). Poor outcomes did not differ between patients operated on by interventionalists with >2-year experience (5.5%, 18/330) and <2-year experience (6.6%, 11/166, P=0.60). The following factors were tested for as predictors of outcome: age, sex, ruptured aneurysm status, Hunt and Hess grade, aneurysm location, aneurysm size, prior aneurysm treatment, operator experience, type of stent, stenting technique, staged treatment, procedural complications, immediate aneurysm occlusion, and delivery of coils before stent placement. Patient age (>65 years; P<0.001), ruptured aneurysm status (P<0.001), Hunt and Hess Grades 4 to 5 (P<0.001), procedural complications (P<0.001), posterior circulation aneurysms (P=0.01), female sex (P=0.06), and single-stage SAC (P=0.01; caused by inclusion of all ruptured aneurysms in this group) were predictors of unfavorable outcome (GOS I-III). In multivariable analysis, patient age (OR=0.9; 95% CI, 0.92–0.99; P=0.04), ruptured aneurysm status (OR=0.01; 95% CI, 0.002–0.07; P<0.0001), and procedural complications (OR=0.02; 95% CI, 0.004–0.1; P<0.001) were the only independent predictors of unfavorable outcome.

Aneurysm rupture after successful treatment was noted in only 1 patient (0.2%, 1/496; with a previously unruptured stent-coiled aneurysm arising from the vertebral artery). Another patient (0.4%, 1/263) scheduled for staged coiling after successful stent placement suffered a subarachnoid hemorrhage and expired.

Discussion
In this study, we assessed the safety and long-term efficacy of SAC of complex intracranial aneurysms. Given the large sample size of our study, we were able to detect several independent predictors of complications, immediate occlusion, recanalization, and outcome. Our study has also afforded an opportunity to compare treatment outcomes between open- and closed-cell stent designs and address important questions such as the need and safety of staging SAC, the feasibility of stenting in the acute setting of subarachnoid hemorrhage, and the optimal SAC technique.

Procedural complications occurred in only 6% of patients in this series causing death or permanent morbidity in 3%, which confirms the safety of stent-assisted techniques for treatment of intracranial aneurysms. Of note, we used the number of patients treated as our denominator to assess for complications. Had we used the total number of procedures, our denominator would have risen to 760 and our procedural complication rate would have been 4.5%. The morbidity and mortality rates in our series are largely in line with previously reported SAC series. Using Neuroform stents, Lessne et al reported a 5.4% rate of thromboembolic events, whereas Fiorella et al noted periprocedural strokes in 6.7% of patients causing death in 1.8%. Maldonado et al reported a 2.9% combined morbidity and mortality rates after Neuroform SAC of 76 aneurysms. Likewise, in the multicenter Enterprise registry, procedural data demonstrated a 6% temporary morbidity, 2.8% permanent morbidity, and 2% mortality. Because of the closed-cell design of the Enterprise stent, concerns have been raised regarding its conformability and vessel wall apposition, with the potential for thrombotic events. Heller et al found that incomplete stent apposition as assessed by 3-T MR angiography was more prevalent in Enterprise (55%) versus Neuroform stents (0%) and was also associated in 80% of cases with periprocedural ipsilateral hyperintense lesions on diffusion-weighted imaging. The results of our study, however, show that complication rates do not differ between open- and closed-cell stent designs. Stent design also did not affect initial occlusion rates or ultimate patient outcomes.

Several techniques of SAC are currently used including the microcatheter jailing technique, the coil through the struts technique, and the coil then stent technique. Interestingly, our study demonstrates that the latter technique where stent deployment follows coil embolization is associated with significantly higher complication rates (16% versus 6.3%) than the other 2 techniques where stents are delivered first. Moreover, in multivariable analysis, the odds of developing complications were 5× greater when coils were delivered before stents. Because the coil then stent technique may involve balloon inflation at the neck of the aneurysm, with stents often deployed in the event of coil prolapse into the parent vessel or an unstable coil mass, thromboembolic complications may be more likely to occur. The higher complication rate could also be related to the lack of pretreatment with antiplatelet agents when stent placement had not been anticipated.

Some operators advocate staging the stent-coil procedure to allow endothelialization of the stent. This may theoretically allow for greater stability and lesser movement of the stent during coil deployment. However, staged SAC did not confer any benefit for procedural complications or angiographic outcomes in this study. Also, staged treatment was associated with lower initial aneurysm occlusion rates in multivariable analysis. One patient (0.4%) expired in the waiting period because of interval aneurysm rupture and 2% of patients underwent stent placement but did not return for the second stage of the procedure.

Most operators are reluctant to use antiplatelet therapy in the setting of subarachnoid hemorrhage, because of the potential need for a ventriculostomy, the potential for infarction secondary to vasospasm, and the high likelihood of future invasive interventions. For these reasons, stenting is generally avoided in acutely ruptured aneurysms in favor of clip ligation or other endovascular techniques that do not mandate dual antiplatelet therapy. Indeed, the present study demonstrates that stenting of acutely ruptured aneurysms is
associated with higher thromboembolic and hemorrhagic complications compared with unruptured aneurysms (25% versus 4.7%). Ruptured aneurysms were also independently predictive of complications and poor outcomes. Likewise, other groups have reported that SAC of ruptured aneurysms is associated with increased morbidity and mortality. Thus, the safety-efficacy profile of SAC is clearly less favorable in ruptured than in unruptured aneurysms. In some patients with acutely ruptured aneurysms, however, SAC is the only available treatment option. In this case, SAC can be undertaken with acceptable morbidity and mortality (12.7%) and provides favorable outcomes in >50% of patients as suggested by the present study. Previous series have also shown the feasibility of SAC of acutely ruptured aneurysms, namely larger parameter and precipitate saccular thrombosis and endothelialization across the neck of the aneurysm. Some predictors of sac of acutely ruptured aneurysms.22 In a systematic review of the literature that included 339 patients, Bodily et al19 found clinically significant intracranial hemorrhagic complications in 8% of patients and clinically significant thromboembolic events in 6%. The authors concluded that although adverse events were more common with stenting, thromboembolic complications were reasonably well-controlled and ventriculostomy-related hemorrhagic complications were uncommon.

The long-term rates of aneurysm recanalization and retreatment were low in the present study (12% and 6.4%, respectively) suggesting that SAC is an effective and durable treatment for complex intracranial aneurysms. The fact that the Neuroform stent was an independent predictor of recanalization is a potentially crucial finding that has not been previously reported. The published literature on SAC may also suggest such a trend. The retreatment rates with the Neuroform stent were reported to be 14% by Santillan et al20 and 15.1% by Fiorella et al12 versus only 8.3% in the Enterprise registry.21 We suspect that the closed-cell design of the Enterprise stent may more efficiently alter intra-aneurysmal hemodynamic parameters and precipitate saccular thrombosis and endothelialization across the neck of the aneurysm. Some predictors of aneurysm recanalization with SAC seem to be similar to those previously reported with unassisted coiling, namely larger aneurysms and incomplete initial aneurysm occlusion.22 Our study has also identified older age and recurrent aneurysms after previous embolization as strong independent predictors of recanalization with SAC. The association between aneurysm recanalization and increasing age is interesting and probably reflects a weaker neointimal response induced by stent deployment in older patients.

A substantial number of patients in this series underwent aneurysm treatment with a telescoping stent technique. No procedural complications were noted in this group, but occlusion rates at follow-up were suboptimal (21%) and in almost 42% of cases there was an increase or no change in aneurysm size. Clearly, dedicated flow diverters such as the pipeline embolization device provide superior occlusion rates in this setting.23,24 In a recent multicenter study from Hong Kong, Yu et al25 reported complete aneurysm occlusion in 55% at 6 months, 81% at 12 months, and 84% at 18 months after treatment with the pipeline embolization device. Although a safe treatment modality, the telescoping stent technique has largely been supplanted by flow diverters.

Limitations
Our study is limited by its retrospective design and absence of randomization between study groups. The results reflect the experience of a single neurovascular center with specific technique and anticoagulation protocols and may not be readily generalizable to other centers. Because diffusion-weighted imaging was not routinely performed after SAC, the incidence of clinically silent infarcts has likely been underestimated. Despite these limitations, this large study addresses several questions that have not been properly investigated in previous reports and identifies several independent predictors for complications, occlusion, recanalization, and outcome.

Conclusions
Stent-assisted coiling of intracranial aneurysms is safe, effective, and provides durable aneurysm closure. Stent delivery before coil deployment reduces the risk of procedural complications. Staging the stent-coil procedure carries a low risk of interval aneurysm rupture and loss to follow-up and may not improve procedural safety. SAC of ruptured aneurysms is associated with worse outcomes but has an acceptable safety profile. The type of stent used does not affect complication rates or patient outcomes. However, closed-cell stents are associated with significantly lower aneurysm recanalization rates. Older patients have higher aneurysm recanalization rates after SAC.

Disclosures
None.

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