Endovascular Treatment of Unruptured Intracranial Aneurysms With Guglielmi Detachable Coils
Short- and Long-Term Results of a Single-Centre Series

Harald Standhardt, MD, PhD; Hans Boecher-Schwarz, MD; Andreas Gruber, MD; Thomas Benesch, PhD; Engelbert Knosp, MD; Gerhard Bavinzski, MD

Background and Purpose—Purpose of the present study is to evaluate the clinical outcome of endovascular treatment of unruptured intracranial aneurysms and to address the question of long-term stability and protection against future subarachnoid hemorrhage.

Methods—Retrospective analysis of all patients treated in a 12-year period (173 patients: age 26 to 76 yr, mean 52.2±10.8/202 aneurysms: size 3 to 50 mm, mean 10.0±8.3).

Results—The mortality was 0.5%; the overall morbidity was 3.5%. The most frequent complications were thromboembolic events (10.9%). Of these, 3.0% of patients suffered a stroke, leading to severe disability in 1 patient (0.5%). In 1 patient, the aneurysm ruptured during treatment, resulting in relevant neurological disability. Another patient suffered a fatal aneurysm rupture hours after treatment. The occlusion rate depended on aneurysm and neck size. Follow-up angiography revealed a decrease of the occlusion rate over time. This trend was obvious in all size categories and was most pronounced in giant aneurysms. In 3 patients (1.5%) with partially thrombosed giant aneurysms of the posterior circulation, embolization could not prevent later aneurysm rupture. There were no ruptures of any other aneurysms in the follow-up period (3.7±3.4 yr).

Conclusion—Endovascular treatment is a highly safe procedure with low intervention-related morbidity and mortality. Long-term data for nongiant aneurysms showed good protection against rupture in the observation period. In contrast, the risk of rupture for giant aneurysms of the posterior circulation was as high as expected in observational studies. (Stroke. 2008;39:899-904.)

Key Words: intracranial aneurysm ■ endovascular treatment ■ outcome ■ subarachnoid hemorrhage

In 1991, Guglielmi introduced electrolytically detachable platinum coils to occlude cerebral aneurysms through an endovascular approach.1 In the following years it became a widely used therapy for microsurgically “difficult-to-treat” aneurysms, mainly of ruptured aneurysms of the posterior circulation.2–3 The safety and efficacy of this new approach have also made it an attractive treatment option for aneurysms in other locations, and it has been adopted by a steadily increasing number of centers. The recently published International Subarachnoid Hemorrhage Trial (ISAT) documented its efficacy in the treatment of ruptured aneurysms of the anterior circulation.1–5 The significantly better outcome compared to microsurgical clipping resulted in a further boom of endovascular therapy, although long-term results are still lacking and there are many concerns in the scientific community.6

Because very little data concerning the endovascular treatment of unruptured intracranial aneurysms (UIAs) are available to date,7–8 our study evaluated the results obtained in a large series over a 12-year period at a single center. Short- and long-term clinical and anatomic outcomes are reported. Special attention is paid to procedure-related complications and their neurological consequences, and the question of long-term stability and protection against future SAH is addressed. This seems especially important because the natural history of UIAs and the risks of treatment are not absolutely clear. As a consequence there is widespread disagreement over the optimal management of these lesions.

Materials and Methods

Subjects and Methods

A retrospective analysis was undertaken for all patients with saccular intradural UIAs who received endovascular treatment in our department between February 1992 and August 2004, using Guglielmi detachable coils (GDC, Boston Scientific). Patients with fusiform and complex aneurysms that were treated by parent artery occlusion or stenting were not included. The endovascular technique used has been described elsewhere.3
Altogether 202 unruptured cerebral aneurysms in 173 patients were treated. There was a clear female predominance: 73.4% women versus 26.6% men. Patients’ ages ranged from 26 to 76 years with an average age of 52.2 ± 10.8 years (Table 1).

Clinical presentation was as follows: 48.0% of aneurysms were detected incidentally during neuroradiological imaging because of an unrelated medical condition such as cerebrovascular ischemia (10.3%), headache (9.9%), dizziness (4.0%), unexplained collapse (4.0%), epilepsy (4.0%), head trauma (3.0%), or brain tumor (2.5%); 29.7% were identified after the patient had suffered an SAH from another aneurysm, these patients were electively treated after full recovery of the mass effect of the aneurysm; 4.5% were found in addition to an arteriovenous malformation, and 4% were discovered during the screening for an incidental aneurysm because of a family history of SAH.

All patients’ data—hospital files, operative reports, and outpatient charts collected during clinical routine by members of the department—were evaluated to screen for procedure-related morbidity and mortality. This information was supplemented by follow-up clinical examinations and telephone interviews to detect possible aneurysm rupture after treatment. This was done by one of the authors of the study.

Clinical outcome was rated according to the Modified Ranking Scale (mRS). To calculate the overall procedural complication rate, all interventions regarding the endovascular treatment were evaluated: initial endovascular treatment, subsequent endovascular retreatments, and angiographic follow-up. The complication rate was calculated per treated aneurysm.

The diagnostic, postprocedural, and follow-up angiograms were reviewed by one of the authors to obtain the degree of aneurysm occlusion. Obliteration was classified as: complete obliteration; neck remnant (residual neck rest but more than 90% obliteration); incomplete occlusion (contrast filling of the aneurysm sac or obliteration less than 90%).

Aneurysm dimensions and location were determined (Tables 1 and 2; Figure). The size of the treated aneurysms ranged from 3 to 50 mm with a mean diameter of 10.0 ± 8.3 mm. Aneurysm size was classified into the same 4 groups as for ISUIA 2003,8 aneurysm neck was considered narrow if <4 mm and wide if ≥4 mm. Aneurysm dimensions were measured with the angiography equipment, and size was estimated through comparison with the diameter of the parent vessel and the coil size used. In addition, size was evaluated by CCT, CT angiography, or MR tomography.

### Table 1. Patient Demographics and Aneurysm Dimensions

<table>
<thead>
<tr>
<th>Patient’s age</th>
<th>Mean ± SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age distribution</td>
<td>52.2 ± 10.8</td>
<td>26</td>
<td>76</td>
</tr>
<tr>
<td>&lt;40</td>
<td>21 (12.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–69</td>
<td>137 (79.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td>15 (8.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46 (26.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>127 (73.4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Aneurysm Location

<table>
<thead>
<tr>
<th>Location</th>
<th>Anterior circulation</th>
<th>Posterior circulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>87 (43.1%)</td>
<td>43 (21.3%)</td>
</tr>
<tr>
<td>ICA/bifurcation</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>ICA/supracranial</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>ICA/ACoA</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ICA/PCoA</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>ICA/ophthalmic-paracranial</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>ICA/C3–C4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>ACA</td>
<td>6 (3.0%)</td>
<td></td>
</tr>
<tr>
<td>MCA</td>
<td>36 (17.8%)</td>
<td></td>
</tr>
<tr>
<td>VBJ</td>
<td>2 (1.0%)</td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>32 (15.8%)</td>
<td></td>
</tr>
<tr>
<td>BA/bifurcation</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>BA/SCA</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>PCA</td>
<td>3 (1.5%)</td>
<td></td>
</tr>
</tbody>
</table>

ICA indicates internal carotid artery; ACoA, anterior choroidal artery; PCoA, posterior communicating artery; ACoA, anterior communicating artery; ACA, anterior cerebral artery; MCA, middle cerebral artery; VA, vertebral artery; PCA, posterior inferior cerebellar artery; VBJ, vertebro-basilar junction; BA, basilar artery; SCA, superior cerebellar artery; PCA, posterior cerebral artery.

For statistical analysis a general linear model was used, P < 0.05 was considered significant. Statistical calculations were carried out using SAS Version 8 (SAS Institute Inc).

### Indications for Aneurysm Treatment

Patients with UIAs were normally referred to the outpatient clinic of our neurovascular service after detection of the aneurysm at another institution. There treatment options for every individual patient were carefully assessed, and therapeutic alternatives were discussed, including microsurgical clipping and conservative medical management. Before FDA approval in 1995 endovascular treatment was usually advised for surgically unfavorable aneurysms such as giant aneurysms, intracranial aneurysms, partly extradurally located intracavernous aneurysms, or aneurysms in the posterior circulation. Other indications for coiling included a previous failed microsurgical attempt, refusal of surgery, poor medical condition, or age over 70. Later coiling was also offered to patients where either endovascular or microsurgical treatment seemed appropriate. By this time the GDC technique was already well established in our department.

Over time there was a steady increase in the percentage of UIAs treated by coiling compared to microsurgical clipping. In recent years endovascular therapy has become the first choice treatment provided the aneurysm geometry is suitable for this treatment modality.

### Follow-Up Protocol

After discharge patients were followed up by our outpatient clinic. Follow-up of patients from distant locations was sometimes handled by their referring local neurosurgical department. In such cases follow-up angiograms and clinical information were forwarded for evaluation.

Follow-up angiography was scheduled 6 to 12 months after embolization. If a stable result was demonstrated, another angiography was advised 2 to 3 years postembolisation. Further angiogra-
Thromboembolic and hemorrhagic events were identified as complications leading to neurological dysfunction.

Thromboembolic incidents occurred in the treatment of 22 aneurysms, but were tolerated without lasting neurological sequelae in the majority of cases. Six patients suffered a permanent neurological deficit attributable to a thromboembolic event. One of these patients, who had systemic lupus erythematosis and developed an antiphospholipid syndrome, suffered a major stroke (mRS 4). The other 5 made a good clinical recovery: 3 had no significant disability despite symptoms (mRS 1), and 2 were left with only slight disability (mRS 2). A TIA occurred in 8 patients between 2 and 2 weeks after the intervention, usually on the day of treatment. Two patients suffered a PRIND; both made a fast clinical recovery and were neurologically intact at discharge. In another 6 patients thromboembolic arterial branch occlusion in the depending territory was visible during the intervention; 4 of them needed intraarterial thrombolytic therapy to regain vessel patency; all patients were neurologically asymptomatic after terminating general anesthesia. Coil dislocation out of the aneurysm into the parent vessel was the second most frequent complication. In only 2 patients this led to a TIA attributable to a thromboembolic incident.

Table 4. Procedure-Related Complications

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic events</td>
<td>22</td>
<td>10.9%</td>
</tr>
<tr>
<td>Stroke</td>
<td>6</td>
<td>3.0%</td>
</tr>
<tr>
<td>Minor deficit</td>
<td>5</td>
<td>2.5%</td>
</tr>
<tr>
<td>Major deficit</td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td>PRIND</td>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td>TIA</td>
<td>8</td>
<td>4.0%</td>
</tr>
<tr>
<td>Clinically silent</td>
<td>6</td>
<td>3.0%</td>
</tr>
<tr>
<td>Coil dislocation</td>
<td>8</td>
<td>4.0%</td>
</tr>
<tr>
<td>Arterial dissection</td>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td>Aneurysm perforation</td>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td>Aneurysm rupture</td>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td>Vascular access sheath</td>
<td>3</td>
<td>1.5%</td>
</tr>
<tr>
<td>Anaesthesia-related problem</td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>19.3%</td>
</tr>
</tbody>
</table>

In 202 treated aneurysms, 40 complications occurred in 39 patients (1 patient suffered 2 complications).
There were 2 aneurysm perforations (1.0%) during intervention. The first patient developed a posthemorrhagic hydrocephalus and needed a temporary external ventricular drainage. The patient recovered completely (mRS 0). Another patient had guidewire perforation near the aneurysm neck. Emergency microsurgical clipping led to an excellent clinical recovery. Two patients suffered a procedure-related aneurysm rupture (1.0%). In one a malpositioned coil was repositioned by means of a balloon. During this maneuver the aneurysm ruptured. Despite acute clipping the patient was left with severe disability (mRS 4). The other patient suffered an SAH 8 h after the intervention and subsequently died. In this very early case a giant superior cerebellar artery aneurysm was only partially obliterated, because of the supply of large coils was insufficient.

Three patients had problems related to the vascular access sheath (1.5%). There was one retroperitoneal bleeding, requiring substitution of the erythrocytes. Occlusion of the common femoral artery was diagnosed on follow-up in another patient without clinical symptoms. In the third case, a femoral artery occlusion required acute intervention through vascular surgery to prevent permanent sequelae. One patient had a temporary respiratory problem after termination of anesthesia (0.5%). There were 2 catheter-induced dissections of cervical arteries without clinical consequences.

Follow-Up and Long-Term Results of Treatment

Long-Term Clinical Result

Clinical follow-up was available for 190 of 199 aneurysms (95.5%). Mean follow-up was 3.7±3.4 years, ranging from 3 months up to 11.8 years (follow-up >2 years: 59.8%; >5 years: 32.1%; >10 years: 6.5%), representing a total of 708 aneurysm-years.

During follow-up in 2 patients a proven SAH occurred. The first patient had a partially thrombosed giant vertebrobasilar junction aneurysm. Treatment in 1994 resulted in high-grade occlusion. In 1998 the patient hemorrhaged (clinical state Hunt & Hess 1) and a new aneurysm fundus could be occluded again with coils. The patient made an excellent recovery, but repeated reperfusion of the aneurysm and coil compaction led to subsequent stent implantation combined with coiling in 2003. The second patient had a symptomatic, partially thrombosed giant basilar bifurcation aneurysm. Embolization resulted in 90% occlusion, but control angiography six months later showed compaction of the coils and large reperfusion. Microsurgical clipping was advised but the patient refused surgery. Clinical symptoms progressed, and 21 months after the initial treatment she died from an SAH. A third patient with a giant basilar bifurcation aneurysm had a good clinical outcome after embolization. Later an obstructive hydrocephalus required ventriculoperitoneal shunting. Two and a half years after embolization she died of unknown causes. No autopsy was performed, but rupture of the aneurysm must be assumed.

These 3 aneurysms represent 37.5% of the 8 giant aneurysms of the posterior circulation. The mean follow-up of this subgroup was 3.3±2.9 years, ranging up to 9.5 years, and the cumulative follow-up was 26.0 aneurysm-years. Rupture of the aneurysms occurred between 18 and 52 months after initial treatment. The calculated annual risk of rupture is 11.5% per year.

In contrast to giant aneurysms of the posterior circulation, none of the giant aneurysms of the anterior circulation ruptured. To our knowledge, there has been no rupture of a nongiant aneurysm in our patients to date.

Long-Term Anatomic Result

Angiographic follow-up was available for 151 of 199 aneurysms (79.9%). Mean follow-up was 2.9±2.8 years, ranging up to 11.8 years (follow-up >2 years: 42.7%; >5 years: 19.1%; >10 years: 4.0%). Follow-up angiography revealed a decrease of the occlusion rate over time (Table 3). The overall rate of complete occlusion declined from 57.5% to 47.9%. The proportion of aneurysms with a neck remnant fell from 34.0% to 23.9%, whereas the percentage of incompletely obliterated aneurysms increased from 8.5% to 28.2%. This trend was obvious in all size categories and was most pronounced in giant aneurysms.

Repeated embolization was carried out in 23 of 199 aneurysms (11.6%) after demonstrated reperfusion or growth of the aneurysm during follow-up. The number of interventions increased with the size of the aneurysm (small 1.02; medium 1.03; large 1.70; giant 1.89). In 8 aneurysms (6 small: 6.8%; 2 giant: 10.8%) microsurgical clipping was performed because of reperfusion or growth of the aneurysm; 3 aneurysms were treated by parent artery occlusion. All together, 32 aneurysms received additional treatment (16.1%).

Discussion

Aneurysmal SAH is a devastating disease with high morbidity and mortality even today. Despite many improvements in the management of ruptured aneurysms, the estimated mortality rate remains approximately 50%, and a morbidity rate of 20% to 25% after SAH can be expected. Moreover, a large percentage of patients considered to have made a good clinical recovery according to conventional neurological outcome scales will show significant impairment in cognitive or psychosocial function and quality of life. Therefore, preventive treatment of patients harboring UIAs seems essential to avoid the horrendous consequences of SAH.

Until recently, clipping of UIAs was a straightforward decision. But data demonstrating a lower risk of rupture and a higher risk of treatment than generally assumed called this strategy into question. As a result, whether elective treatment should be offered to these patients became the subject of continuing controversy, leaving clinicians and patients with the dilemma of whether to treat or not to treat.

In parallel to the endovascular treatment of ruptured aneurysms, coiling of UIAs evolved as an obvious minimally invasive alternative to microsurgical clipping, one that would probably be better tolerated by the patient.

Most published studies on the safety and efficacy of endovascular treatment had been carried out on ruptured aneurysms in patients after an SAH, and treatment results were extrapolated to the management of unruptured aneurysms even though proof of its long-term efficacy was not yet available. Robust data concerning the treatment of UIAs...
were not available.\textsuperscript{7–8} Only in the last few years have several publications addressed the question of safety and efficacy of endovascular treatment of UIAs,\textsuperscript{18–19} But the information available today is still based on a small number of treated patients, and data on the long-term stability and protection against SAH are lacking.\textsuperscript{8} As future prevention of SAH is the primary goal of treatment, the availability of these data is vital.

**Risk of Treatment**

In the present study the overall procedure-related mortality was 0.5%, and the permanent morbidity was 3.5%: 2 patients were left with severe disability (1.0%), and the other 5 patients had a good outcome despite treatment-induced neurological deficit (2.5%). All other patients had an excellent outcome (mRS 0).

This morbidity and mortality rate is in the range of previously published single-center studies on UIAs that report mortality rates from 0% to 2.5% and morbidity rates from 1.4% to 5.5%. In the only existing meta-analysis on the endovascular treatment of unruptured aneurysms to date, Lanterna et al\textsuperscript{8} calculated a mortality rate of 0.6% for 1379 available patients; the average morbidity rate was 7.0% based on 794 available patients. This complication rate is comparable to that of the endovascular treatment of ruptured aneurysms.\textsuperscript{20}

Prospective multi-center and retrospective community-based studies reported a significantly higher treatment-induced complication rate. Two community-based studies found adverse events in more than 10% of treated patients although the mortality rate was low.\textsuperscript{21–22} In ISUIA, the prospectively evaluated mortality rate was 3.4% and the morbidity was 6.4%.\textsuperscript{9} One reason for the higher morbidity and mortality reported in these studies could be a publication bias in single-center studies that may underestimate the complication rate of a technique.\textsuperscript{23} The higher morbidity rate reported in ISUIA is possibly related to the inclusion of cognitive assessment in the study design, whereas cognitive status and psychosocial functioning are usually not systematically evaluated in the single-center studies, although impairment in these areas can sometimes impair quality of life even more than physical disability. Nor were these areas systematically evaluated in our study, and underestimation of the risk of treatment cannot be excluded. Therefore the thorough assessment of these qualities in future prospective studies seems mandatory.\textsuperscript{11}

In their meta-analysis, Lanterna et al found a significantly decreased complication rate in recent years. The morbidity rate was 8.6% in older studies, whereas for recent studies an average morbidity of only 4.5% was found. A reduction in the risk of treatment was also evident in our study ($P=0.015$). All major complications occurred in the early years of the study period. In the last 5 years there was no procedure-related mortality, and only one patient was left with a mild neurological deficit (mRS 1). The decrease in the complication rate reflects the learning curve of the endovascular team and the multiple technical advances that were introduced over the years (improved interventional imaging quality, improved catheters and guidewires, softer and more versatile coils, optimized anticoagulation regimes, new drugs for the management of thromboembolic events).

**Long-Term Stability and Effectiveness of Treatment**

The goal of treatment of UIAs is the prevention of rupture and subsequent SAH. The effectiveness of the procedure must therefore be defined as the reduction in the incidence of SAH compared to the natural history of unruptured aneurysms. Whether long-term protection against SAH is achieved by endovascular treatment is not clear because there are almost no data available to date on this issue.\textsuperscript{7–8} The reports in the literature about rupture of coiled, previously unruptured aneurysms have to be called anecdotal and the follow-up of the published series on unruptured aneurysms unfortunately is short and often incomplete. The bleeding rate of ruptured aneurysms after endovascular intervention is somewhat better documented and in larger series was about 1% in the first year after treatment.\textsuperscript{5,17} But even these studies provide no long-term data.

Lanterna et al found 13 postembolisation bleedings in 703 patients in 30 studies included in their analysis. The average follow-up of the single studies ranged from 0.5 to 3.8 years, the mean follow-up of all studies was 2.0 years, representing 1416 patient-years. Lanterna et al calculated an overall annual bleeding rate of 0.9%. This rate seems relatively high compared to the annual bleeding risk for unruptured aneurysms found in observational studies. In their analysis only partially occluded aneurysms larger than 10 mm had bled. For 85 aneurysms larger than 10 mm they found an annual bleeding rate of 3.5%.

In our study there were 2 proven cases of SAH during follow-up. In addition there was another patient where death because of the rupture of the treated aneurysm has to be assumed. All patients had giant aneurysms of the posterior circulation, and none of these aneurysms could be occluded completely through embolization. The calculated annual risk of rupture for this subgroup is 11.5% per year, and is similar to that reported by ISUIA,\textsuperscript{9} which estimated the risk of rupture for this group at 10% per year. This result is even more disappointing as multiple interventions were necessary during follow-up. Consequently, GDC embolization of this group of aneurysms has to be strongly questioned. Modified endovascular treatment strategies such as stent-assisted coiling, or future developments such as bioactive coils, might help to attain better results. But as long as there is no better long-term stability on the horizon for this group, well-established techniques such as microsurgical clipping or parent artery occlusion seem appropriate, if technically feasible.\textsuperscript{24}

In contrast to the poor long-term result in giant aneurysms of the posterior circulation, there were no ruptures in any other aneurysm group. Clinical follow-up was available for almost all patients (95.5%), and the cumulative follow-up was 708 aneurysm-years. Although follow-up was up to more than 11 years, the mean follow-up of 3.7 years is still short and longer observation periods are needed to answer this question definitively.

As demonstrated also by others,\textsuperscript{25} long-term stability cannot be achieved for all aneurysms treated by coiling. In the
present study a trend toward reperfusion was obvious for all groups of aneurysms. Aneurysm diameter and neck size were found to impact on long-term stability. Angiographic follow-up of treated patients therefore seems mandatory as partially occluded aneurysms might be at risk of future rupture. In the case of relevant aneurysm reperfusion, additional coiling, microsurgical clipping, or parent artery occlusion should be considered.

Summary

Our study found coiling to be a highly safe therapy with almost nonexistent morbidity and mortality in recent years. The long-term data for nongiant aneurysms give rise to the hope that the primary goal of treatment, the prevention of SAH, can be achieved. The good risk/benefit ratio therefore appears to justify treatment. Whether life-long protection can be obtained remains uncertain.

For giant aneurysms of the posterior circulation long-term results were disappointing, and a reduced risk of rupture through coiling has to be questioned. Well-established treatment alternatives such as microsurgical clipping or parent artery occlusion must be considered.

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Disclosures

None.

References

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