Evidence Table

Clinical Area: Endovascular treatment of intracranial aneurysms


Study Type: Case series.
Study Aim: To determine the safety and efficacy of the Onyx liquid embolic system in treating difficult intracranial aneurysms.

Outcomes

Primary: Occlusion of the aneurysm, neurologic morbidity, and other adverse events.

Design

- Number of subjects: N= 97 patients with 100 aneurysms in the CAMEO study, and N=100 in Cekrige study (36 patients overlapped in the two series)
- Description of study population: CAMEO trial: The study enrolled patients from 20 European centers. 79% females, median age 46 years (mean 45 years, range 6-76 years), and 17.5% presented with subarachnoid hemorrhage (SAH), 10 % <1months, and 7% >1 months. 10% of the patients were treated within 1 months of the SAH, 90% were treated for unruptured, or recurrent aneurysms. 29% were incidental, and 46% were associated with mass effect. 15% were previously treated with coils, 3 with stent, 2 with wrap, and none had a previous surgical clipping. 21% had small aneurysms (<10mm), 60% had large aneurysms 10-25 mm, and 19% had giant aneurysms >25 mm. The median aneurysm sizes were 15 mm for the dome height, 14 mm for the dome width, and 7mm for the neck width. 93% were in the carotid territory, and 7% in the posterior circulation. Cekirge et al's series: mean age 41 years (range 6-71), 16 had SAH. 28% of all aneurysms were incidental, and 72% were associated with headache and/or mass effect and seizures. 65% were small aneurysms and 35% were giant or large/ wide necked. 98% were in the carotid territory, and 2% in the posterior circulation
- Method of subject selection (inclusion/exclusion criteria): 1. Aneurysms likely to be difficult to treat or that presented high risk for conventional coil techniques or neurosurgical clipping, 2. Aneurysms that had recurred after a previous coil embolization, and 3. Had failed to respond to prior surgical or endovascular treatment.
- Consecutive patients? Yes.
- Exposure/Intervention: 108 Onyx treatments according to the standard procedures were performed to treat 100 aneurysms in 97 patients. The treatment was then
followed with angiography to confirm the satisfactory or complete occlusion of the aneurysm. Adjunctive stents were used in 175 of cases in the first procedure, and in 5% in a retreatment procedure.

- **Source of outcome data (e.g. patient self-report, doctor report, lab results):** Clinical data were collected before, at time of the procedure, at discharge, and after 3 and 12 months of follow-up. This included the collection of Glasgow outcome score, modified Rankin scale, and cranial nerve deficits.

- **Length of follow-up:** 12 months in CAMEO trial, and up to 5 years in Cekrige et al’s series.

- **Completeness of follow-up:** 67% complete in the CAMEO trial.

**Validity**

- **Is the study type appropriate for the question(s) being asked?** No, a randomized controlled trial comparing the treatment to an alternative therapy would be more appropriate.

- **Were patients similar with respect to baseline characteristics?** No.

- **Was the intervention and other aspects of patient care similar for all patients (or for all patients in a defined subgroup)?** No, the procedures were performed in different centers by 24 physicians, some patients received adjunctive stents, and the procedure time, experience, and the range of balloons available changed along the study.

- **Was the process of observation likely to affect the outcome?** Not for the objective outcomes.

- **Did an objective observer assess outcomes and were outcome measurements consistent?** Yes.

- **Was follow-up duration appropriate?** No not for determining long-term efficacy.

**Conclusions regarding validity of methods:**

This is a small case series that lacked a control or comparison group.
Results:

_Angiographic outcomes immediately after, And at 3 and 12 months after the procedure (CAMEO trial)_

<table>
<thead>
<tr>
<th></th>
<th>Small &lt;10 mm</th>
<th>Large 10-24 mm</th>
<th>Giant 25 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Immediately after embolization</td>
<td>N=20</td>
<td>N=60</td>
<td>N=19</td>
</tr>
<tr>
<td>Complete occlusion (100%)‡</td>
<td>15</td>
<td>33</td>
<td>9</td>
</tr>
<tr>
<td>Subtotal occlusion (90-99%)</td>
<td>5</td>
<td>23</td>
<td>9</td>
</tr>
<tr>
<td>Incomplete (&lt;90%)</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3-6 months follow-up**‡</td>
<td>N=15</td>
<td>N=51</td>
<td>N=15</td>
</tr>
<tr>
<td>Complete occlusion (100%)</td>
<td>13</td>
<td>31</td>
<td>8</td>
</tr>
<tr>
<td>Subtotal occlusion (90-99%)</td>
<td>1</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Incomplete (&lt;90%)</td>
<td>1</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Not determinable</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>12 months follow-up***‡</td>
<td>N=14</td>
<td>N=39</td>
<td>N=14</td>
</tr>
<tr>
<td>Complete occlusion (100%)</td>
<td>13</td>
<td>30</td>
<td>8</td>
</tr>
<tr>
<td>Subtotal occlusion (90-99%)</td>
<td>0</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Incomplete (&lt;90%)</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Not determinable</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

* After treatment when applicable

_The complete occlusion rate in Cekirge et al’s series_

At post randomization 97%, 78% and 76% in the small, large and giant aneurysms respectively
At 3-6 months; 100%, 62% and 65% respectively
At 2-5 years (n=58): 100%, 100% and 93% respectively.

_Rankin score at discharge and at 3 and 12 months after the procedure for patients with available data (KAMEO trial)_

_Rankin scale_  
Unruptured and other

At discharge (n=87)  
- Rankin score 2 or better  88%
- Unchanged /Improved  87.2 %
- Worsened %  9.3 %
- Death at discharge  3.5 %

At 3-6 months (n=82)  
- Rankin score 2 or better  90%
- Unchanged /improved  90.2 %
- Worsened %  9.3 %
- Death at discharge-3 months  0.0 %

At 12 months or last follow-up (n=83)  
- Rankin score 2 or better  79%
- Unchanged /improved  90.0 %
- Worsened %  3.6 %
- Death at 3-12 months  2.4 %

There were some missing data
For the 10 patients with recent SAH, the great majority had an unchanged or improved scale

<table>
<thead>
<tr>
<th>Adverse events (KAMEO trial)</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events*</td>
<td>26</td>
<td>26.8</td>
</tr>
<tr>
<td>Procedure and device related adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious groin complications**</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Device related events</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Permanent neurologic damage</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Death***</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

* Includes visual loss, cranial nerve palsy, hemiparesis, worsening of neurologic status, stroke, and infarct.
** Resulted in death of one patient
*** 7 patients died during the period of the study but not all were related to the procedure.

Follow-up angiography was performed annually in Cekirge et al’s series and showed that 12/96 (12.5%) aneurysms recanalized during follow-up. (36% in the large or giant groups)

**Authors’ Conclusions:**

The authors of CAMEO trial concluded that Onyx treatment offers an endovascular alternative for selected patients with intracranial aneurysm unsuitable for coil treatment or who have failed a previous therapy.

Cekirge and et al, concluded that Onyx provides durable aneurysm occlusion with parent artery reconstruction resulting in perfectly stable 1-year to 5-year follow-up angiography.

**Reviewer’s Conclusions:**

These overlapping series were relatively small, conducted among selected groups of patients, and had and no control or comparison group. The results of CAMEO trial show a high complete occlusion rate at 12 months follow-up (93% for smaller aneurysms, 77% for the large, and 57% for the giant aneurysms). Cekirge et al reported a complete occlusion rate at 2-5 years among 100% for the small and large aneurysms, and 93% for the giant aneurysms. The observed recanalization rate was 12.5% after 2-5 years of follow-up.