Efficacy and complications of endovascular embolization for very small (3 mm or smaller) ruptured cerebral aneurysms

Kei HARADA\textsuperscript{1)} Kousuke KAKUMOTO\textsuperscript{3)} Youhei OONAKA\textsuperscript{3)} Shingo YAMASHITA\textsuperscript{4)} Yuuichirou TAMAOKI\textsuperscript{1)} Haruto FUJIMURA\textsuperscript{1)} Takashi YOSHIDA\textsuperscript{1)} Kenji UDA\textsuperscript{4)} Katsuaki GUNGE\textsuperscript{2)} Shogo OSHIKATA\textsuperscript{1)} Masahito KAJIHARA\textsuperscript{2)}

\textsuperscript{1)}Department of Neurosurgery, Fukuoka Wajiro Hospital
\textsuperscript{2)}Department of Neurosurgery, Fukuoka Shin-Mizumaki Hospital
\textsuperscript{3)}Department of Neurosurgery, Shin-Takeo Hospital
\textsuperscript{4)}Department of Neurosurgery, Shin-Yukuhashi Hospital

\textbf{Objective}: Endovascular embolization of very small aneurysms (under 3 mm in maximum diameter) is considered to be high risk for aneurysm perforation.

\textbf{Methods}: We compared initial angiographic results of ruptured aneurysms between under 3 mm in diameter (21 cases, small group) and over 3 mm in diameter (85 cases, non-small group), the results of short-term follow-up angiography in the small group were also demonstrated. In the small group, extremely soft coils were mainly used for aneurysmal filling.

\textbf{Results}: The technical success rates in the small and in the non-small groups were 95.2\% and 100\%, respectively. Initial angiographic results showed that complete occlusion was obtained in 65.0\% of the small group and 52.9\% of the non-small group. The mean packing densities in the small and non-small groups were 47.1\%±11.4\% and 26.4\%±9.5\%, respectively, showing the packing density in the small group was significantly higher than those in the non-small group (p<0.001). Intra-operative aneurysmal perforation occurred in 14\% and 2.4\% in the small and non-small groups, respectively (p=0.08), but none resulted in neurological worsening. In the small group, post-operative rupture occurred in 5\%. Follow-up angiography was performed in 12 cases (60\%) at 3–12 months after the procedure, and complete occlusion was obtained in 92\%.

\textbf{Conclusion}: Endovascular embolization of very small aneurysms is more likely to result in intra-operative aneurysmal perforation compared to larger aneurysms. The use of extremely soft coils could obtain a high packing density, and suitable for repairing these perforations.

\textbf{Key words}: subarachnoid hemorrhage, small aneurysm, endovascular treatment

\textsuperscript{1)}Kei HARADA, 2-2-75 Wajirogaoka, Higashi-ku, Fukuoka, Fukuoka 811-0213, Japan  E-mail: keihara@f-wajirohp.jp

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Diagram of endovascular embolization procedure.}
\end{figure}

\section*{Introduction}

During the past decade, there has been significant development in the treatment of cerebral aneurysms.\textsuperscript{1,3)} However, very small aneurysms (less than 3 mm in maximum diameter) are reported to have a higher potential risk of perforation since there is less space within the aneurysm to insert the microcatheter and anchor the coils.\textsuperscript{4,5)} In the International Subarachnoid Aneurysm Trial, such very small aneurysms were not included, and it concluded that endovascular coiling was not a preferred treatment to apply to these very small aneurysms.\textsuperscript{6)} Recently, extremely soft coils have been developed for use as filling and finishing coils in cerebral aneurysms. As a
result, these soft coils have made the packing aneurysms safer, and the packing density has increased because there is less microcatheter kickback during coil insertion into the aneurysms. Especially, they have been frequently used for embolization of ruptured small aneurysms. The purpose of this study is to examine the clinical efficacy and safety for the treatment of ruptured very small aneurysms.

Materials and Methods

1. Patient background and characteristics

From April 2010 to March 2013, we performed endovascular coil embolization of 106 aneurysms in 106 consecutive patients with ruptured cerebral aneurysm. These cases were considered suitable for embolization after evaluation by neurosurgeons and neurointerventionalists. Endovascular embolization was applied to the patients with small aneurysms for the following reasons: poor grade, aneurysm located mainly in posterior circulation, or advanced age. The patients included 77 women (72.6%) and 29 men (27.4%) with a mean age of 63.7 years (range, 29–87 years). The neurological condition was severe with a World Federation of Neurosurgical Societies (WFNS) grade 4–5 in 38 (34.2%) patients. We divided the patients into two groups. The small group comprised patients with aneurysms under 3 mm (maximum diameter), while the non-small group included patients with aneurysms over 3.1 mm. The background of the patients as well as aneurysm characteristics in both the groups is summarized in Table 1.

2. Endovascular treatment

In most cases, the GDC-18 360 and GDC-10 360 (Boston Scientific, Natic, MA, USA), the Target-10 360 (Stryker, Kalamazoo, MI, USA), or Trufill Orbit (Cordis, Johnson & Johnson, Fremont, CA, USA) 3D coils were used as framing coils at the initiation of embolization. The ED coil-10 Extra Soft (EDC-10 ES; Kaneka Medix Corporation, Osaka, Japan) were mainly used in the middle and later stages of the procedure, and they were mostly used as finishing coils in the final stage of embolization. The Hyperform (eV3 Covidien, Irvine, CA, USA) or Hyperglide (eV3 Covidien) balloons were used in the balloon-assist technique.

3. Angiographic evaluation

The method of angiographic evaluation was described previously. A 3D angiogram was recorded immediately after treatment and at follow-up (BRANSIST Safire, Shimadzu, Kyoto, Japan). The size of aneurysms in three planes (height, length, and width) was measured on the 3D angiograms with reference markers included in the view. The maximum aneurysm size was defined as the longest dimension. The aneurysm sac volume was calculated using the following equation:

<table>
<thead>
<tr>
<th></th>
<th>Small (≤3 mm)</th>
<th>Non-small (&gt;3 mm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61.1±10.4</td>
<td>64.4±10.8</td>
<td>0.31</td>
</tr>
<tr>
<td>Sex, female</td>
<td>18 (86%)</td>
<td>59 (69%)</td>
<td>0.18</td>
</tr>
<tr>
<td>WFNS Grade</td>
<td></td>
<td></td>
<td>0.80</td>
</tr>
<tr>
<td>I-III</td>
<td>9</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>IV, V</td>
<td>12</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Aneurysmal location</td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>14</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>7</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Size (mm)</td>
<td>2.70±0.31</td>
<td>8.17±3.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Volume (mm³)</td>
<td>6.7±2.1</td>
<td>306.8±204.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dome/neck ratio</td>
<td>1.72±0.35</td>
<td>1.93±0.65</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Aneurysmal sac volume \(= \frac{4}{3} \pi \times \frac{\text{length}}{2} \times \frac{\text{width}}{2} \times \frac{\text{height}}{2}\)

The volume of the inserted coil was calculated as follows:

Coil volume \(= \pi \times \left(\frac{\text{diameter of coil}}{2}\right)^2 \times \text{length of coil}\)

Packing density (%) was calculated by dividing the volume of inserted coils by the volume of the aneurysm \(\times 100\).

The neck size indicates the length of the aneurysm orifice plane and the dome size was obtained by measuring the distance between the orifice plane and the fundus of the aneurysm. The degree of aneurysmal occlusion was graded using a modified three-point Raymond score (RS), where RS1 indicates complete obliteration of the aneurysm and neck; RS2 indicates small neck remnant without contrast filling of the aneurysm sac; and RS3 indicates contrast filling of the aneurysm sac.

4. Statistical analysis

The small and non-small groups were compared using the statistical analysis software ystat2013 (Igakutosho-shuppan Ltd, Tokyo, Japan). The unpaired 2-group t test was performed to determine differences according to age, aneurysmal size, volume, ratio of its dome/neck, and packing density. Chi-square analysis and the Fisher exact probability test were performed for categorical variables. A value of \(p<0.05\) was considered significant.

Results

1. Initial angiographic and clinical results and complications

Initial angiographic and clinical results, and follow-up results are summarized in Table 2. Adjuvant techniques, such as the balloon-assist and double-catheter methods, were used in 19% of the small group, which were significantly lower than their use in 54% of the non-small group (\(p<0.01\)).

The technical success rates in the small and non-small groups were 95.2% and 100%, respectively. Initial angiographic results showed that the sac and neck were completely occluded in 65.0% and 52.9% of the small and non-small groups, respectively, and graded as RS1 score. Four patients (20%) in the small group were graded as RS2 and 3 patients (15%) were graded as RS3, while 27% of the patients were graded as RS2 and 20% of the patients were graded as RS3 in the non-small group. Complete occlusion was not achieved in 35.0% and 47.1% of the small and the non-small groups, respectively. The state
of embolization in the small and non-small groups had no statistical differences \( (p=0.25) \). The mean packing density was 47.1±10.7\% and 26.4±9.5\% in the small and non-small groups, respectively, and it was significantly higher in the small group than that of the non-small group \( (p<0.001) \).

In the small group, 65\% achieved RS1 with mean packing density of 51.2±10.0\%, while 35\% of patients with RS2 or 3 had a mean packing density of 39.6±7.4\%.

Procedural complications were observed in 19.0\% and 4.7\% of the small and non-small groups, respectively, and these were significantly higher in the small group than in the non-small group \( (p=0.04) \). Intra-operative aneurysmal rupture was higher in the small group \( (3/21, 14\%) \) than in the non-small group \( (2/85, 2.4\%) \), with no statistical difference \( (p=0.08) \). Table 3 shows the aneurysmal characteristics and follow-up results of the small group by case. In the small group, all intra-operative aneurysmal perforations occurred during the simple technique. Two aneurysms were perforated by the microcatheter, and one aneurysm was perforated by the finishing coil. In case 3, the aneurysmal perforation was caused by the microcatheter before coil placement (Fig. 1). In case 6, the aneurysmal perforation was occurred by the microcatheter after the detachment of the first coil (Fig. 2). In these cases, the extremely soft coils were deployed both outside and inside of the aneurysm during embolization of the perforated site of the aneurysm. In case 21, the aneurysmal perforation was caused by the third coil of the extremely soft coil. There was no case with post-operative massive hematoma according to CT, and no neurological deterioration occurred. In the non-small group, two intra-operative aneurysmal perforations occurred. One aneurysmal perforation occurred in the case with anterior communicating artery (Acom) aneurysm using simple technique. The aneurysm was perforated by a microcatheter after placing the first coil, and later another microcatheter was navigated to manage the aneurysm. The other aneurysmal perforation occurred in case with the internal carotid artery aneurysm using balloon-assist technique. The aneurysm was perforated by a microcatheter during the placement of the first coil, additional coils were placed immediately after the detachment of the first coil with balloon inflation. Both cases had no massive intracranial hemorrhages on post-operative CT. Cerebral embolism during the procedures occurred in 4.7\% and 2.4\% of the small and non-small groups, respectively, but there were no statistical differences \( (p=0.89) \).

During the follow up, post-operative rerupture occurred in 5\% of the small group, and none in the non-small group. In case 19, with an Acom aneurysm, the post-operative aneurysmal rerupture occurred 14 days after the procedure (Fig. 3), and the patient died without additional surgical or endovascular treatment. There was no retreatment within 1 year in the small group.

2. Short-term angiographic outcomes in the small group

Follow-up angiographies were performed in 12 cases \( (60\%) \) at 3–12 months after the procedure. Eight of 12 aneurysms \( (66.7\%) \) initially scored with an RS1 were stable, and the other 4 cases were dropped out of the follow-up. Of the 4 aneurysms which initially scored an RS2, 2 aneurysms improved to RS1, 1 aneurysm was stable, and 1 was dropped out of the follow-up. Of the 3 aneurysms initially scored as an RS3, 1 improved to an RS2, 1 improved to an RS3, 1 improved to an Rs2, 1 was dropped out of the follow-up, and 1 had been reruptured.

Discussion

Coil embolization for very small aneurysms is considered to be technically challenging due to the risk of potential aneurysm perforation during the procedure.\(^{5,9,10}\) Since very small aneurysms do not have enough space for the insertion of the microcatheter and coils, a direct force either through the microcatheter or the coil may cause aneurysm wall perforation.\(^{10,11}\) In this study, intraprocedural rupture occurred in 14\% in the small group and 2.4\% in the non-small group. The rupture rate was similar to those obtained from previous studies. In endovascular embolization of very small ruptured aneurysms, the occurrence rate of aneurysmal ruptures was higher than that in larger aneurysms.\(^{4,12}\) In the meta-analysis reported by Brinjikji, et al., procedural rupture of very small aneurysm was 8.3\%, and other studies reported to be 0–16.7\%.\(^{4,5,10,13}\) Nguyen, et al reported a 5-fold increase in the incidence of procedural rupture during coil embolization of the aneurysms less than 3 mm in...
### Table 3  Initial and follow-up results of the small group

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, year</th>
<th>Sex</th>
<th>Location</th>
<th>Size (mm)</th>
<th>Dome/neck ratio</th>
<th>Volume (mm³)</th>
<th>Method</th>
<th>Type of coil used</th>
<th>Packing density (%)</th>
<th>RS</th>
<th>Complication</th>
<th>Follow up (month)</th>
<th>mRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70</td>
<td>F</td>
<td>MCA</td>
<td>3.0</td>
<td>1.5</td>
<td>7.4</td>
<td>S</td>
<td>ED 2.5/6</td>
<td>32.3</td>
<td>2</td>
<td></td>
<td>1 (3)</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>F</td>
<td>Acom</td>
<td>3.0</td>
<td>1.5</td>
<td>6.3</td>
<td>S</td>
<td>GDC-10 soft 360 2/4, ED 1.5/3</td>
<td>53.3</td>
<td>1</td>
<td></td>
<td>1 (12)</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>F</td>
<td>Distal ACA</td>
<td>2.5</td>
<td>2.2</td>
<td>4.2</td>
<td>S</td>
<td>ED 2/4*, 1.5/1</td>
<td>48.4***</td>
<td>2</td>
<td>Perforation</td>
<td>none</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>M</td>
<td>MCA</td>
<td>3.0</td>
<td>1.7</td>
<td>9.0</td>
<td>S</td>
<td>ED 2.5/4, 2/3, 1.5/2</td>
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<td></td>
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</tr>
<tr>
<td>5</td>
<td>50</td>
<td>F</td>
<td>Distal ACA</td>
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<td>2.0</td>
<td>6.3</td>
<td>S</td>
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<td>3</td>
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<td>0</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
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<td>Acom</td>
<td>2.8</td>
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<td>10.7</td>
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<td>Orbit 2.5/4.5, ED 2/4*, 2/3, 1.5/2</td>
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<td>Perforation</td>
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</tr>
<tr>
<td>7</td>
<td>69</td>
<td>F</td>
<td>BA top</td>
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<td>1.5</td>
<td>6.3</td>
<td>S</td>
<td>GDC-10 soft 360 2/4, ED 1.5/2</td>
<td>48.4</td>
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<tr>
<td>8</td>
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<td>Acom</td>
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<td>5.2</td>
<td>S</td>
<td>GDC-10 soft 360 2/4</td>
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<td>1</td>
<td>died</td>
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<td></td>
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<tr>
<td>9</td>
<td>56</td>
<td>F</td>
<td>IC-AchoA</td>
<td>2.0</td>
<td>1.3</td>
<td>4.2</td>
<td>S</td>
<td>ED 2/3, 1.5/2</td>
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<tr>
<td>10</td>
<td>54</td>
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<td>Acom</td>
<td>2.5</td>
<td>1.7</td>
<td>6.5</td>
<td>S</td>
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</tr>
<tr>
<td>11</td>
<td>63</td>
<td>F</td>
<td>BA-SCA</td>
<td>3.0</td>
<td>1.5</td>
<td>7.5</td>
<td>S</td>
<td>GDC 10 soft 360 2/4, ED 1.5/2, 1.5/2</td>
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<td>MCA</td>
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<td>1.4</td>
<td>6.3</td>
<td>S</td>
<td>ED 2.5/4, 1.5/2</td>
<td>48.3</td>
<td>3</td>
<td></td>
<td>2 (6)</td>
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</tr>
<tr>
<td>13</td>
<td>56</td>
<td>F</td>
<td>IC-AcoA</td>
<td>2.9</td>
<td>2.0</td>
<td>6.3</td>
<td>Bal</td>
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</tr>
<tr>
<td>14</td>
<td>77</td>
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<td>Acom</td>
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<td>9.8</td>
<td>S</td>
<td>Orbit 2.5/4.5, DeltaPlash 2/2, 2/2</td>
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<tr>
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<td>43</td>
<td>F</td>
<td>PICA</td>
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<td>S</td>
<td>ED 2/3, 1.5/2, 1.5/2</td>
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<td>BA top</td>
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<td>1.3</td>
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<td>Bal</td>
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<td>1</td>
<td>died</td>
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</tr>
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<td>17</td>
<td>78</td>
<td>F</td>
<td>BA-SCA</td>
<td>2.8</td>
<td>1.5</td>
<td>7.9</td>
<td>Bal</td>
<td>Target-Helical 2/4, ED 2/3</td>
<td>45.2</td>
<td>2</td>
<td>Left occipital infarction</td>
<td>1 (12)</td>
<td>2</td>
</tr>
<tr>
<td>18</td>
<td>82</td>
<td>F</td>
<td>Distal ACA</td>
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<td>1.5</td>
<td>7.9</td>
<td>S</td>
<td>ED 2.5/6, 1.5/2, 1.5/2, 1.5/1</td>
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<td>1</td>
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<td>5</td>
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<tr>
<td>19</td>
<td>60</td>
<td>M</td>
<td>Acom</td>
<td>2.7</td>
<td>1.3</td>
<td>9.0</td>
<td>S</td>
<td>Target-Ultra 360 2.5/4, ED 2/2</td>
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<td>3</td>
<td>Rerupture (Day 14)</td>
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</tr>
<tr>
<td>20</td>
<td>41</td>
<td>F</td>
<td>BA-SCA</td>
<td>2.0</td>
<td>2.0</td>
<td>2.3</td>
<td>Bal</td>
<td>Target-Ultra 360 2/4, ED 1.5/1, 1.5/1***</td>
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<td>Not successful, clipping</td>
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<tr>
<td>21</td>
<td>61</td>
<td>F</td>
<td>A1</td>
<td>2.5</td>
<td>2.0</td>
<td>5.0</td>
<td>S</td>
<td>Target-Ultra 360 2/4, ED 1.5/1, 1.5/1***</td>
<td>40.3</td>
<td>2</td>
<td>Perforation</td>
<td>2 (6)</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 1
A: Pre-operative angiography of case 3 revealed a distal anterior cerebral artery aneurysm. During the navigation of the microcatheter, aneurysmal dome was perforated by the microcatheter.
B: Extremely soft coil was placed outside the aneurysm; the microcatheter was pulled into the aneurysm and the coil was then placed into the aneurysm, and additional filling coil was placed. Final angiography revealed neck remnant of the aneurysm.

Fig. 2
A: Pre-operative angiography of case 6 revealed an anterior communicating artery aneurysm.
B: The first coil was placed.
C: After detachment of the first coil, microcatheter perforated the aneurysm spontaneously; arrow indicates the tip of the microcatheter.
D: Extremely soft coil was placed outside the aneurysm, the microcatheter was pulled into the aneurysm, and the coil was then placed into the aneurysm. Final angiography revealed complete occlusion of the aneurysm.
comparison with larger aneurysms; 11.7% of aneurysms less than 3 mm and 2.3% of larger aneurysms. The first generation of GDC coil, which was the most popular coil, had a tendency of catheter kickback; the microcatheter was pushed back out of the aneurysm sac during insertion of the last portion of the coil, and had a risk of perforating the aneurysm when reinsertion of the microcatheter into its previous position was attempted. van Rooji, et al. reported that they preferred to occlude a small aneurysm with just one coil and strived to choose the most appropriate coil length between 1 and 8 cm that would accommodate and occlude the aneurysm. They reported 196 cases of aneurysms of less than 3 mm, which were coiled during a period between 1995 and 2008; the microcatheter kickback prevented the insertion of more coils. In the present series, 3 aneurysmal perforations occurred; 2 aneurysms were perforated by microcatheter and 1 was made by the filling coil. The cause of aneurysmal perforation was thought to be due to the difficulty of control of the microcatheter, and over packing of the filling coils. In case 3 and 6 of the present series, difficulty of microcatheter control was a major cause of aneurysmal perforation due to the long access root of the distal anterior cerebral artery aneurysm, and steep angle of Acom and parent artery. In case 21, over packing of the filling coils may cause an aneurysmal rupture.

**Fig. 3**
A: Pre-operative angiography of case 19 revealed anterior communicating artery aneurysm. 
B: Final angiography revealed dome filling of the aneurysm.
C, D: Rerupture occurred 14 days after the procedure, and angiography showed refilling of the aneurysm and pseudo-aneurysm.
The recent development of extremely soft coils for cerebral aneurysms may achieve tight packing of small aneurysms. The EDC-10 ES is a bare platinum coil with excellent handling properties that may be suitable for embolization of small aneurysm. This coil is extremely soft with an unprecedentedly small diameter of the element wire (0.0014 inches) and very flexible pusher wire system, which may prevent microcatheter kickback. Additionally, the EDC-10 ES has the lowest profile of 1.5 mm in diameter and the smallest length of 1 cm, which could fill the small gaps in the coil mass. In the present series, EDC-10 ESs were used in 80% of cases.

Extremely soft coils were also useful for repairing perforation of the aneurysms. When the microcatheter perforated the aneurysm, the tip of the coil was initially placed outside the aneurysm, the microcatheter was then pulled into the aneurysm, and the residual part of the coil was placed into the aneurysm. In the present series, this technique was used for repairing 2 cases of microcatheter-induced perforations (cases 3 and 6, Fig. 1, 2). Extremely soft coils were easier to use than other coils because of its softness and less potential for kickback.

Generally, a packing density of more than 25% for embolization of cerebral aneurysms has a low tendency of recanalization. However, packing density of about 25–30% for small aneurysms could not be achieved always. In the present series, complete occlusion (RS1) was achieved in 65%, while neck remnant (RS2) and dome filling (RS3) was seen in 35% of the small group. In the small group, the mean packing density was 51.2% in RS grade 1 aneurysms and 39.6% in RS2 and RS3 aneurysms. Case 19 of Acom aneurysm resulted in dome filling (RS3) with a packing density of 33.6%, subsequently rerupture occurred 14 days after the procedure (Fig. 3). In this case, loose packing might have caused rupture.

In this study, the balloon-assist technique was applied in only 19% of the patients in the small group and 44% in the non-small group. This technique may prevent massive hemorrhage when the aneurysm is ruptured during embolization. However, the movement of microcatheter can be affected by the assist balloon at the orifice of the aneurysm. Gupta, et al. reported that manipulation of the balloon had to be done with care so as to prevent sudden movement of the microcatheter tip. The balloon inflation should be avoided during the coil placement so as to allow microcatheter movement, except when the coil tip or loop tended to prolapse out of the aneurysm when it ruptured. In the present series, we prepared the assist-balloon by using 6 French guiding catheters in 13 cases in order to navigate rapidly to the orifice of the aneurysm when it ruptures. The double-catheter technique is not suitable for small aneurysms, because the small aneurysms do not have enough space to position two microcatheters. In ruptured small aneurysms with a narrow neck, even a regular
microcatheter blocked the aneurysmal inflow as seen in case 10 of the present series (Fig. 4).

The limitation of this study is a small number of cases based on a short-term follow-up period. Long-term follow-up may be required to evaluate the long-term safety of the coil embolization of ruptured small aneurysms.

Conclusion

Endovascular embolization of very small aneurysms is more likely to result in intra-operative aneurysmal perforation compared to larger aneurysms. The use of extremely soft coils may contribute to obtain high packing density, and suitable for repairing these perforations.

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None.

References


