Evaluation of Endovascular Embolization of Cerebral Aneurysms by Hydrogel Coils

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Summary

Background: Hydrogel coils were created to improve the chances of an effective endovascular treatment of cerebral aneurysms. Achieving a high packing density of coils in the lumen of aneurysms can decrease the risk of recurrence. The aim of the present study is to report our initial experience on the effectiveness and safety of endovascular treatment of intracranial aneurysms with the use of hydrogel coils.

Material/Methods: Sixty patients (age: 28–72 years) (45 women, 15 men) were treated. In 18 patients (30%), subarachnoid hemorrhage was present. Digital subtraction angiography (DSA) of cerebral vessels with rotational scanning was performed. Image analysis was performed by the Philips Integris 3D RA device, which is a specialized workstation (Three-Dimensional Rotational Angiography). 3D reconstructions of cerebral arteries were created based on the data. Sixty-six cerebral aneurysms were embolized with hydrogel coils, which expand in contact with blood, reaching the maximum diameter in about 20 minutes. In 29 aneurysms (43.9%), the effect of the procedure was confirmed on a follow-up DSA after 8.0±4.1 months from the initial treatment.

Results: A complete embolization was performed in 55 aneurysms (83.3%), and partial embolization in 11 aneurysms (16.7%). In 6 aneurysms (9.1%), re-embolization was necessary and it resulted in a complete embolization of 5 aneurysms. On a follow-up DSA, complete embolization was present in 25 aneurysms (86.2%), and partial embolization in 4 aneurysms (13.8%), respectively.

Conclusions: Endovascular embolization with hydrogel coils is an effective and safe treatment method for cerebral aneurysms, although it carries the risk of some complications.

MeSH Keywords: Embolization, Therapeutic • Hydrogel • Intracranial Aneurysm

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Background

Recent studies have reported a high prevalence of cerebral aneurysms in the general population [1–3]. Some of the aneurysms can rupture causing subarachnoid hemorrhage (SAH). This hemorrhage can result in death in about 12% of patients even before admission [4]. Among those who are hospitalized, about 40% die within one month. More than one third of the remaining patients will have a major neurological deficit [5]. Asymptomatic aneurysms constitute a considerable challenge for clinicians who qualify patients for the treatment, because it is difficult to predict which aneurysms have a higher risk of rupture and hemorrhage [3]. It is suggested that the risk of hemorrhage is related to the age of the patient, hypertension, location and size of the aneurysm [3,6,7]. Some studies recommend to treat intracranial aneurysms bigger than 7mm, however smaller aneurysms can also cause subarachnoid hemorrhage [7].
Endovascular treatment of intracranial aneurysms is a widely used alternative to traditional surgery, which is reported by many authors [8,9]. According to the International Subarachnoid Aneurysm Trial (ISAT) – a randomized controlled trial of 2143 patients with cerebral aneurysms, comparing neurosurgery with endovascular treatment, better clinical outcomes were obtained in the latter method. Within 9 years of follow-up in this study, there was an increased risk of recurrent bleeding in the endovascular group compared to the neurosurgery group. However, the risk of death within 5 years after treatment was significantly lower in the endovascular group compared to the neurosurgery group [10]. On the other hand a recent Polish study assessing the long-term results of microsurgical and endovascular therapy for intracranial aneurysms in patients with subarachnoid hemorrhage showed that the outcomes in both methods were comparable, and embolization was associated with a higher rate of complications in the elderly [11].

Endovascular embolization is more comfortable for the patients, however, high rates of re-treatment and recurrence have been reported [12]. The suspected major causes of recurrence include the diameter of aneurysmal neck, sac-to-neck ratio [13] and a low initial packing density of coils inside the aneurysm [14,15]. Hydrogel coils were developed to increase the packing density and consequently the chances of effective endovascular treatment of cerebral aneurysms [16]. Hydrogel-coated coils consist of a platinum coil covered with a hydrophilic polymer that absorbs water and swells when immersed in blood. The swelling of coils should result in an improved aneurysm filling in comparison to traditional coils. The recent preliminary studies have supported this hypothesis, providing good evidence that hydrogel coils allow a substantially improved packing of the aneurysmal lumen when compared to standard platinum coils, which was associated with reduced rates of recurrence [16–19].

Based on the above-described observations, we hypothesized that endovascular treatment of cerebral aneurysms with hydrogel coils can be an alternative to traditional surgery and to other endovascular methods. Therefore, the aim of the present study is to report our initial experience regarding the effectiveness and safety of the endovascular treatment of intracranial aneurysms with hydrogel coils.

**Material and Methods**

This prospective study was approved by the institutional ethics committee. All 60 patients (45 women, 15 men) with 66 intracranial aneurysms who were treated with hydrogel coils from January 2010 to March 2012 were included in the analysis. The mean age was 53.0±11.0 years (range: 28 to 72 years). The inclusion criteria were: 1. Intracranial aneurysm diagnosed on angiography or CTA or MRA, either ruptured or unruptured; 2. Decision of an experienced interventional radiologist or neurosurgeon that endovascular treatment is an appropriate method of treatment; 2. Contraindications to administer medications necessary for the embolization procedure; 3. Coagulopathies; 4. Pregnancy or lactation; 5. Age lower than 18 years; 6. Lack of patient’s consent.

Digital subtraction angiography (DSA) of cerebral vessels with rotational scanning was performed in 60 patients to assess aneurysms. Image analysis was made in a specialized workstation (Philips Integris 3D RA, Three-Dimensional Rotational Angiography). 3D reconstructions of cerebral arteries were created based on the data. The length, width and height of the aneurysms as well as the diameter of the aneurysmal neck were measured based on the surface-shaded display (SSD) reconstructions.

Sixty-six cerebral aneurysms were embolized. They were of various sizes (mean maximum diameter: 7.1±4.4 mm, range: 2.5 to 27 mm), of various neck diameters (<4 mm – 27.3%, ≥4 mm – 72.7%) and were found in a variety of locations in the posterior (16.6%) and anterior (83.4%) brain circulations. The aneurysms represented all clinical grades from asymptomatic (23.0%) to those associated with acute subarachnoid hemorrhage (30.0%). Detailed characteristics of the treated aneurysms are presented in Table 1. Six aneurysms needed secondary embolization due to recanalization, coil mesh, aneurysm regrowth or neck enlargement. In the rest of cases, only one endovascular procedure was performed. The procedures were performed under general anesthesia. In the case of unruptured aneurysms, the patients received aspirin and clopidogrel for 5 days before the intervention. First, platinum coils were positioned inside the aneurysm to create a frame and then hydrogel coils were placed. The closing coils were all platinum due to the fact that these coils are less stiff than hydrogel coils and therefore easier to position. When necessary, the procedure involved balloon remodeling or adjunctive stent placement or papaverine administration. The hydrogel coils were expended by blood. Their maximum diameter should be reached in about 20 minutes. There is also a limited time of 5 minutes for the positioning and retraction of these coils. Angiograms were taken after positioning the last coil and after 20 minutes. The occlusion of the aneurysm was assessed based on the Montreal Scale (class 1 – the best desired therapeutic effect, class 2 – lack of packing in the neck of aneurysm 3 – residual aneurysm, presence of any amount of contrast medium inside aneurysmal lumen) [20].

**Follow-up**

All patients were invited for a follow-up examination. Of the 29 aneurysms (43.9%) in 27 patients (45.0%), follow-up angiography was performed after 8.0±4.1 months after the initial treatment. As initially, the occlusion of the aneurysm was assessed based on the Montreal Scale [20]. Recurrence was defined as any increase in the size of remnant on follow-up [13].

**Statistical analysis**

Statistical analysis was performed with the STATISTICA 9.0 PL software package. The results were presented as: mean ± standard deviation or range for the normally distributed data and percentages for nominal and ordinal. The
assessment of the normal distribution was based on the Shapiro-Wilk test. To compare the effect of embolization directly after treatment and on follow-up, the Wilcoxon test was used. The results were considered as statistically significant with a p value lower than 0.05.

**Results**

Sixty-six intracranial aneurysms were embolized in 60 patients. The Montreal class 1 was present in 55 aneurysms (83.3%), class 2 in 5 aneurysms (7.6%) and class 3 in 6 aneurysms (9.1%). In case of 6 aneurysms (9.1%), remodeling was necessary and it was performed with the achievement of Montreal class 1 in 5 aneurysms and class 2 in 1 case. The mean number of hydrogel coil used was 6±3 (range: 2 to 12). The procedure involved remodeling in 21 patients (35%) – 6 balloon remodeling and 15 adjunctive stent placement. Papaverine was administered during 11 (15.3%) embolization procedures. In total, 72 embolization procedures were performed – in 49 patients – one procedure, in 10 patients – two procedures and in 1 patient – three procedures.

We observed the following complications during embolization - a temporary constriction of blood vessel – 13 cases (18.1%), rupture of aneurysm – 2 cases (2.8%), coil mesh – 1 case (1.4%), thrombosis in a blood vessel – 1 case (1.4%), large hematoma in the area of injection to a blood vessel – 1 case (1.4%), death – none.

**Follow-up**

A follow-up angiography was obtained in 27 patients (45%), in 29 aneurysms (43.9%). The Montreal class 1 occlusion was present in 25 aneurysms (86.2%), class 2 – in 2 aneurysms (6.9%) and class 3 – in 2 aneurysms (6.9%). In three aneurysms, the initial class 3 changed into class 1. One aneurysm initially classified as class 3 changed into class 2. In two aneurysms initial class 2 changed into class 1. And two aneurysms initially classified as class 1 changed into class 3. In the rest of the 21 (72.4%) cases, the Montreal class of occlusion was the same as initially. Recurrence rate was 6.9%. There was no statistically significant difference in the class of occlusion on the Montreal Scale between the assessments immediately after the treatment and during the follow-up (p=0.4008).

Figures 1 and 2 show examples of SSD reconstructions from DSA scans of the treated aneurysms before embolization and on the follow-up.

**Discussion**

The present study is one of a few studies that have assessed the effectiveness and safety of endovascular treatment of cerebral aneurysm with hydrogel coils. This unique technology was developed to improve the occlusion of intracranial aneurysms. As soon as the coil is immersed in blood, the hydrogel polymer covering the coil expands about 3 times of its initial diameter. One would therefore expect an increased volumetric filling of the aneurysm and a decreased dependence on thrombus formation, which should reduce the risk of aneurysm recanalization.

There is no endovascular embolization method which can fill an aneurysmal lumen in 100%. It is unavoidable, that around the coils there are unstable thrombi developing. Thrombogenic and thrombolytic processes, among other factors, can cause recurrence of aneurysm. It means that a low aneurysm packing density is related to a bigger, unstable thrombus and consequently to a higher risk of recurrence. This hypothesis is supported by previous studies showing that a low density of coils inside an aneurysm were associated with a higher recurrence rate [13,15]. However, our intention was not to count the packing density; primarily due to the fact that we believe that the expansion of hydrogel is not complete when two hydrogel coil loops touch each other [21]. Another problem is an irregular shape of aneurysms, which usually does not allow for a

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**Table 1. Detailed characteristic of treated aneurysms.**

| Aneurysm size          |          |          |
|------------------------|----------|----------|
| Width of aneurysm [mm] | 6.5±3.6  |          |
| Length of aneurysm [mm]| 7.1±4.4  |          |
| Height of aneurysm [mm]| 7.1±4.1  |          |

| Neck of aneurysm diameters          |          |          |
|-------------------------------------|----------|----------|
| Mean neck width [mm]                | 3.8±1.5  |          |
| Mean neck length [mm]               | 4.3±1.6  |          |
| Narrow neck < 4 mm [N (%)]          | 18 (27.3%)|          |
| Wide neck ≥ 4 mm [N (%)]            | 48 (72.7%)|          |

| Suck to neck ratio                  |          |          |
|-------------------------------------|----------|----------|
| Mean                                 | 1.9±0.9  |          |

| Aneurysm location [N (%)]           |          |          |
|-------------------------------------|----------|----------|
| Anterior brain circulation          | 55 (83.4%)|          |
| Right interior carotid artery       | 21 (31.8%)|          |
| Left interior carotid artery        | 9 (13.7%) |          |
| Right middle cerebral artery        | 4 (6.1%)  |          |
| Left middle cerebral artery         | 6 (9.1%)  |          |
| Anterior communicating artery       | 11 (16.7%)|          |
| Right anterior cerebral artery      | 2 (3.0%)  |          |
| Left anterior cerebral artery       | 1 (1.5%)  |          |
| Pericallosal artery                 | 1 (1.5%)  |          |
| Posterior brain circulation         | 11 (16.6%)|          |
| Basilar artery                      | 7 (10.6%) |          |
| Left posterior communicating artery | 1 (1.5%)  |          |
| Right posterior inferior cerebellar artery | 1 (1.5%) |          |
| Left vertebral artery               | 1 (1.5%)  |          |
| Right vertebral artery              | 1 (1.5%)  |          |
simple volume calculation. Thus, we think that counting packing density for hydrogel coils is a very difficult task.

In a recent meta-analysis by Serafin et al., in which 1683 embolized aneurysms from thirteen studies were included, the pooled rate of initial complete aneurysm occlusion was 59% in the group of aneurysms treated with the use of hydrogel coils. In this group, the pooled total recurrence rate was 17% and the pooled major recurrence rate was 11%. [22]. Moreover, a recent review and meta-analysis of bioactive coils by Broeders et al. showed that hydrogel coils caused a significant reduction of residual aneurysms compared to bare coiling [23]. The high rate of occlusion observed in our study seems to be comparable to the above results.

It should be also emphasized that re-treatment rate in our study (9.1%) was comparable to previous studies. Gaba et al. [17] reported a re-treatment rate of 10% in a group treated by HydroCoils. Similarly, in the study of O’Hare et al. [24], the re-treatment rate was 6.6%. These results seem to be comparable to the re-treatment rates of standard platinum coils [13,17,25].

Gaba et al. [17], in their follow-up angiography, demonstrated a stable obliteration class of 83% aneurysms, which is comparable to our results (72.4%). Furthermore, the recurrence rate of 6.9% observed in our study seems to be also comparable to the 9.5% recurrence rate observed previously by Fanning et al. [25]. Recurrence rates reported in the studies on platinum coils were significantly higher [13,25–27]. However, many factors influencing the effect of embolization (aneurysm location, size, neck’s width, operator experience, using only hydrogel coils or hydrogel coils plus platinum coils as first or last coil) make an objective
comparison between previous studies and our results very difficult, which needs further analysis.

It should be mention that in the case of 6 aneurysms during follow-up, we observed a better occlusion class than initially. Similarly, Berenstein et al. [28] observed this conversion in 60% of aneurysms initially classified as class 3. An improvement in aneurysm obliteration in about 26% of aneurysms, regardless of their size, was also reported by Gunnerson et al. [29]. What is important is that this phenomenon is not common for platinum coils [20,26].

In some patients we saw complications during the embolization procedures. Four of them should be considered as serious. In 2 patients, we caused a rupture of aneurysm with following SAH, however, patients did not suffer from major neurological deficits after treatment. In 1 patient, we caused thrombosis in a blood vessel which was successfully treated by a local administration of thrombolytic agents. Hematoma in the groin area, where the injection was done, was also observed in 1 patient. After a standard treatment, no complications of blood flow in the leg were observed. This complication rate seems to be comparable to the previously published data [22]. For instance, O’Hare et al. [24] reported a complication rate of 16.6%, with 4/5 of complications in their study having occurred during embolization of ruptured aneurysms, the rest, i.e. 1/5 was seen in unrepaired aneurysms. Other possible complications such as septic meningitis and delayed hydrocephalus, described by other authors [24,30,31], did not happen in our study group.

The main limitation of the presented study is a small sample size and the lack of a long-term follow-up. Another important issue is the fact that a significant number of patients (55%) was lost to follow-up. All the treated patients were invited for a follow-up examination. However, only 27 patients reported for a follow-up DSA. The reasons for this cannot be easily explained. Some authors suggest that recanalization is an early problem [17,26,32,33], so that the lack of early recurrence may indicate good long-term outcomes. Nevertheless, this is only an assumption and, to our knowledge, there is still no long-term follow-up in a representative sample of patients treated for intracranial aneurysms with hydrogel coils. Therefore, it seems that further follow-up studies focusing on the effectiveness and safety of hydrogel coil treatment of cerebral aneurysms are needed.

Conclusions

The presented results are comparable to previous studies on Hydrocoils. We obtained a high rate of occlusion. The rate of perioperative complications as well as recurrence and re-treatment rates were relatively low. This allowed us to conclude that endovascular embolization with hydrogel coils seems to be an effective and safe treatment method of cerebral aneurysms, although not without risk of complications.

Statement

All authors confirm that there has been no significant financial support for this study that could have influenced its outcomes.

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