Bare platinum coils vs. HydroCoil in the treatment of unruptured intracranial aneurysms—A single center randomized controlled study

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ABSTRACT

Purpose: The HydroCoil Embolic System (HES) was developed to improve aneurysm filling to provide superior occlusion efficacy, reduce retreatment rates and enhance long-term durability. We performed a randomized clinical trial to compare the effectiveness of bare platinum coils (BPC) vs. HES for unruptured intracranial aneurysms.

Methods: Ninety-six patients underwent endovascular coiling of unruptured intracranial aneurysms. The aneurysms were randomized equally to receive BPC or HES. Immediate angiographic results, number of coils used and complications were evaluated and all cases had 12-month follow-up angiography.

Results: Immediate angiographic results demonstrated that 94.0% of aneurysms treated with HES were completely occluded compared to 76.1% of aneurysms treated with BPC (p = 0.3310). The mean number of coils utilized to fill the aneurysm was significantly lower in the HES arm (5.04 vs. 6.93). Additional adjunctive techniques were performed in 51.1% of all cases. There were seven patients (7.3%) with postoperative complications during the study period. The coil type used during the treatment did not demonstrate any significant differences on the overall recurrence rate (HES – 18.0%, BPC – 17.4%, p = 0.9712). There was a statistically significant difference in the aneurysm size and the neck width between completely occluded aneurysms and aneurysms with residual flow in both immediate angiographic and mid-term follow-up.

Conclusions: Overall, aneurysm size and neck width are the main risk factors associated with aneurysm recurrence. HES compared to BPC required less total number of coils to provide a denser aneurysm filling. However, there were equivocal results with both devices, at the mid-term angiographic follow-up.

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1. Introduction

As in the case of open neurosurgical clipping, the aim of endovascular coiling is to completely exclude the aneurysm from the circulation and to protect against hemorrhage. The basic weakness of endovascular therapy of cerebral aneurysms with coils as compared to surgical clipping is the possible recurrence and potential bleeding [1–3]. On the basis of aneurysm size, morphology, its neck size and location, 4–50% of aneurysms will recur after treatment [4]. Approximately 23% of aneurysms recur after coiling with a re-treatment rate of 15% in the first two years and 1.1% rate of re-rupture [5–7]. Aneurysm recurrence after coiling is basically connected with low density of packing and instability of the coil mass within the aneurysm, defined as volumetric percentage occlusion of the aneurysm cavity with the endovascular device [8–11]. The HydroCoil Embolic System (HES; MicroVention, Aliso Viejo, CA) was designed as a platinum coil coated with a polymeric hydrogel that expands when it contacts aqueous pH balance solution such as blood, to increase filling volumes, improve mesh stability and elicit a healing response within the aneurysm [12]. Although hydrocoils compared to conventional bare platinum coils provide a higher density of packing, delayed complications such as cerebral edema, inflammation, aseptic meningitis and hydrocephalus were reported in patients treated with hydrocoils. These complications are rare and may not be symptomatic, and are therefore hard to detect [13–15]. The design of hydrogel–coated coils is still improving and there are new devices available on the market. Speirs et al. described their initial experiences with HydroFill (MicroVention,
Table 1
Baseline characteristics of patients and aneurysms.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All</th>
<th>HCC</th>
<th>BPC</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>96</td>
<td>50</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>61 (63.5)</td>
<td>31 (62.0)</td>
<td>30 (65.2)</td>
<td>0.7435</td>
</tr>
<tr>
<td>Male</td>
<td>35 (36.5)</td>
<td>19 (38.0)</td>
<td>16 (34.8)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>50.83±9.9</td>
<td>49.6±10.8</td>
<td>52.17±8.7</td>
<td>NS</td>
</tr>
<tr>
<td>Aneurysm size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dome</td>
<td>8.38±4.34</td>
<td>8.32±4.48</td>
<td>8.43±4.45</td>
<td>0.9066</td>
</tr>
<tr>
<td>Neck</td>
<td>4.47±2.28</td>
<td>4.4±2.28</td>
<td>4.5±2.31</td>
<td>0.7553</td>
</tr>
<tr>
<td>Aneurysm location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>75 (78.1)</td>
<td>38 (76.0)</td>
<td>37 (80.4)</td>
<td>0.5995</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>21 (21.9)</td>
<td>12 (24.0)</td>
<td>9 (19.6)</td>
<td></td>
</tr>
<tr>
<td>Bifurcation</td>
<td>43 (44.8)</td>
<td>20 (40.0)</td>
<td>23 (50.0)</td>
<td>0.3250</td>
</tr>
<tr>
<td>Segment of an artery</td>
<td>53 (55.2)</td>
<td>30 (60.0)</td>
<td>23 (50.0)</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD or number (%) is presented; NS = not significant.

Aliso Viejo, CA) and observed 100% immediate angiographic occlusion rate and complete occlusion rate of 86% after a long follow-up period [16].

Due to the fact that recanalization is a major limitation of endovascular methods, the aim of this work was to perform a randomized study comparing hydrocoils with bare platinum coils in the treatment of unruptured cerebral aneurysms.

1.1. The aim

The aim of this single center prospective randomized study was to compare the effectiveness of bare platinum coils vs. HES coils in the treatment of unruptured intracranial aneurysms. Furthermore, mean number of coils used per aneurysm, additional techniques performed, postoperative complications and recanalization risk factors were assessed.

2. Materials and methods

2.1. Study design and population

Patients were recruited and enrolled from the neurosurgery department of the regional medical university. The inclusion criteria included only unruptured intracranial aneurysms. The exclusion criteria included any ruptured aneurysms, intolerance to heparin or resistance to antiplatelet therapy, coagulopathies and abnormal platelet count. The local ethic board approved the study and all patients agreed and signed informed consents to participate.

There were 96 patients (35 male, 61 female, mean age 51) who underwent endovascular intracranial aneurysm repair. Study participants were randomized to statistically equal groups receiving bare platinum coils (BPC group, 46 patients) or hydrogel-coated coils (HES group, 50 patients). To balance group sizes in our study we used one form of restricted randomization: adaptive biased-coin randomization method. Baseline characteristics of patients and aneurysms are shown in Table 1. All procedures were performed percutaneously under general anesthesia by the same experienced neurointerventional radiologist (WP, >10 years practice). Digital subtraction angiography (DSA) control examination was performed immediately after endovascular treatment as the baseline and scheduled after 12-month follow-up period. There was no independent core lab associated with this study but the immediate and follow-up imaging was individually evaluated by the treating physician (WP).

2.2. Interventional procedure and medical therapy

The patients were prepared with a dual antiplatelet therapy (acetylsalicylic acid 75 mg and clopidogrel 75 mg per day) for 5 days before treatment. After the puncture of the common femoral artery and insertion of a 6 F sheath, a bolus of 5000 IU of heparin was administrated intravenously. Then, DSA of both carotid and vertebral arteries was performed. The evaluation of the aneurysm morphology was based on the acquired images and the following features were assessed: dome size, neck width, localization and relation to a parent vessel (Table 1).

During our study, we used various types of 6F guiding catheters (Chaperon, MicroVention, Aliso Viejo, CA; Destination, Terumo, Somerset, NJ; Envoy, Johnson and Johnson, Raynham, MA). In order to exclude the aneurysm from the circulation, a microcatheter (Echelon 10 or Echelon 14, EV3, Plymouth, MN) over a microguidewire (Traxcess, MicroVention, Aliso Viejo, CA; Guide Wire GT 12, Terumo, Somerset, NJ) was positioned within the aneurysm sack and the coils were deployed. According to the randomization, the patients were treated with bare platinum coils or HES. In cases with a wide-necked aneurysm, stent-assisted coiling was performed (Solitaire AB, EV3, Plymouth, MN; Enterprise, Johnson and Johnson, Raynham, MA; Leo+ Balt Extrusion, France) or balloon-assisted (Hypermile or Hyperglide, EV3, Plymouth, MN) coiling technique was used. Before each coil detachment and at the end of the procedure, DSA imaging was performed to assess the parent vessel remained patent and all coils were confined to the target aneurysm. The endovascular embolization procedures were all done under roadmap guidance.

During the time of treatment, special attention was paid to avoid rapid changes in the blood pressure. In cases where a cerebral vasospasm occurred, nitroglycerin was administrated intra-arterially. After the endovascular procedure, the patients were clinically followed by the department of neurosurgery. The patients treated with stent-assisted coiling technique, dual antiplatelet therapy was continued for 3 months, clopidogrel was then discontinued and acetylsalicylic acid was recommended for prolonged period of time. DSA control examination was performed after 12-month follow-up period and compared to the immediate baseline imaging.

2.3. Statistical analysis

Statistica 8.0 software was used to perform a statistical analysis. To analyze categorical data, we used χ² test. Continuous data were analyzed using U Mann–Whitney, Kolmogorov–Smirnow or Kruskal–Wallis tests. The level of statistical significance was p < 0.05.

3. Results

3.1. Immediate angiographic outcome

The aim of any endovascular coiling is complete exclusion of the aneurysm from the cerebral circulation to prevent hemorrhage. In our current study, we achieved total occlusion in 80.2% of all cases and residual neck remnants in 19.8%. The type of the coils did not significantly (p = 0.3310) affect the rate of complete aneurysm occlusion at the end of the procedure (Table 2). However, the use of HES was associated with better total occlusion rate (84.0% vs. 76.1%) and lower residual neck remnants (16.0% vs. 23.9%).

Table 2
Immediate angiographic outcome.

<table>
<thead>
<tr>
<th></th>
<th>HES</th>
<th>BPC</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete occlusion</td>
<td>42 (84.0)</td>
<td>35 (76.1)</td>
<td>0.331</td>
</tr>
<tr>
<td>Residual neck</td>
<td>8 (16.0)</td>
<td>11 (23.9)</td>
<td></td>
</tr>
<tr>
<td>Residual aneurysm</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>

Number (%) is presented.
Immediate angiographic outcome was mainly affected by the size of the aneurysm and the width of the neck \((p < 0.05)\). The mean size of completely occluded aneurysms was 7.81 mm compared to 10.68 mm of the aneurysms with residual neck. Aneurysms totally excluded from the circulation were characterized by the mean neck width of 4.08 mm, whereas in cases with residual neck the mean was 6.26 mm.

### 3.2. Number of coils used

Mean number of coils needed to fill the aneurysm dome was significantly lower while using HES – 5.04 coils per aneurysm in comparison with 6.93 coils per aneurysm in the BPC group. The same results presented as a coil-size unit ratio also showed that HES seems to be a more efficient embolic agent (Table 3). In both groups, the mean number of coils used during the procedure was strongly and significantly correlated with the size of aneurysm dome as well as with the width of aneurysm neck \((p < 0.005)\).

### 3.3. Additional techniques performed

In our study 51.1% of aneurysms required the use of additional adjunctive devices, balloon-assisted coiling was performed in 39.6% of cases, whereas stent-assisted coiling or a combination of both techniques was used in 11.5% of cases. Balloon-assisted coiling was performed more often in the BPC group rather than in the HES group (45.7% vs. 34.0%). On the other hand, the use of stent-assisted coiling or both techniques together was more associated with the HES group (14.0% vs. 8.7%). Embolization without any additional devices was performed in 45.7% of the BPC group and in 52.0% of the HES group. The difference was not statistically significant \((p = 0.4477)\).

### 3.4. Complications

Postoperative complications occurred in seven cases: five in the HES group and two in the BPC group. However, the difference between groups did not reach statistical significance \((10.0\% \text{ vs. } 4.4\%, p = 0.2873)\). The complications directly related to the treatment were two thromboembolic in each arm and one coil displacement in the HES arm. There were no cases of intraprocedural aneurysm rupture. Displaced coil was removed and all four thromboembolic events were managed by mechanical thrombectomy or intra-arterial thrombolysis, but one patient developed an infarct despite treatment. The patient on discharge evaluated on Modified Rankin Scale (mRS) – 3 (moderate disability; requiring some help, but able to walk without assistance), on follow-up examination with mRS – 2 (slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance). There were no cases of periprocedural death. All the patients were discharged in stable condition. In each case, the first clinical follow-up evaluation was planned 3 months after the procedure. If there were any significant symptoms (etc., headache) reported by patient, diagnostic imaging (head CT or MR) was performed. During the 12-month follow-up period we did not observe any post embolization aneurysm rupture, cerebral edema, aseptic meningitis or hydrocephalus.

### 3.5. Mid-term angiographic outcome

DSA control examination performed after 12 months from the initial procedure showed complete occlusion of the aneurysm in 82.3%, residual neck in 9.4% and residual aneurysm in 8.3% of all cases. The difference in total occlusion rate in long-term results between two groups was not statistically significant \((p = 0.9712)\). In the BPC group, there were 38 (82.6%) completely occluded aneurysms, four (8.7%) residual necks and four (8.7%) residual aneurysms. In the HES group, we observed 41 (82.0%) aneurysms completely excluded from the circulation, five (10.0%) residual necks and four (8.0%) residual aneurysms. We treated all the patients with residual flow within aneurysm in both groups. The retreatment rate for HES and BPC was not statistically significant.

### 4. Discussion

Unruptured aneurysms have been exclusively treated in our study. Although several papers have shown that the recurrence of the aneurysm after coiling is associated with the density of packing, there is no literature evidence that there is an increased risk or induction of risk of potential bleeding in regard to the aneurysm recurrence [8–11]. Furthermore, late results of the ISAT study suggest that in ruptured aneurysms this risk is not a danger to jeopardize the overall positive result in terms of outcome in long-term follow-up [17].

Moreover, there is a discrepancy between papers in terms of natural history of unruptured aneurysms less than 7 mm. Based on the second part of the ISUIA study published in 2003, 4060 patients were prospectively analyzed. The cumulative five-year rupture risk factor of hemorrhage from unruptured aneurysms was 0.1% per year in aneurysms less than 7 mm in anterior circulation [18]. These patients probably should be excluded from treatment based on this data. However, there is a discrepancy between the ISUIA study and other clinical studies [19–22]. The Japanese cohort demonstrated that annual rate of rupture per year in unruptured aneurysms in anterior circulation less than 7 mm is 0.75% (95% CI, 0.28–2.02%). Annual risk of aneurysm rupture in different size categories presented in the work of Japanese researchers was much higher than those published in the ISUIA. Aneurysms with an irregular protrusion of the wall were also more likely to rupture [19]. Despite large differences in the estimated risk factor for aneurysm hemorrhage, many authors have indicated for the treatment of aneurysms less than 7 mm in size [20–22].

The design of HES is believed to improve aneurysm filling and therefore provides superior occlusion efficacy, reduce retreatment rates and enhance long-term durability. We conducted a prospective randomized clinical trial on 96 consecutive patients to compare the effectiveness of bare platinum coils vs. HES in the treatment of unruptured intracranial aneurysms.

In our study we observed better, however, not statistically significant, post-treatment complete occlusion rate in the aneurysms.
treated with HES (84.0% vs. 76.1%). Our immediate angiographic results are clearly better than in other studies. Gaba et al. described the series of 60 consecutive aneurysms treated either with HES or standard platinum coils. As in our study, they noted better initial angiographic results in the group treated with HES. However, they achieved lower complete obliteration rates – 58% in the HES group and 53% in the group treated with bare platinum coils. Their results did not reach statistical significance either [23]. In another study performed by Fanning et al. treatment with HES was also associated with better complete occlusion rate. They observed complete occlusion in 28% of the aneurysms treated with HES compared to 10% in the control group. In this case, the results were statistically significant (p = 0.001) [24]. Initial occlusion rate in our study is similar to the Korean prospective multicenter trial of 80 aneurysms in 76 patients treated with HES, in which 75% of the aneurysms were completely excluded from the circulation [25]. We have noted significantly smaller number of coils used per aneurysm while using HES – 5.04 coils per aneurysm in comparison with 6.93 coils per aneurysm in the BPC group (p = 0.003). Interestingly, such findings were not observed in other papers comparing these two types of coils [23,24]. This might have been explained by the tendency of others operators to use shorter HES and/or longer bare platinum coils.

During our study, postoperative complications occurred in five patients (10.0%) in the group treated with HES, two thromboembolic events, one case of pulmonary embolism, one incident of coil displacement and one patient developed pneumonia. In the BPC group, we observed thromboembolic events in 2 (4.4%) patients. The difference between groups did not reach statistical significance (p = 0.2873). On the contrary to our experience, higher incidence of thromboembolic events among patients treated with HES is described in the literature [26]. Recent papers also indicate the association between the use of HES as an embolic agent and the development of aseptic meningitis, perianeurysmal edema and hydrocephalus [27,28]. We did not observe such complications in our cohort. Furthermore, White et al. reported two cases of patients whose aneurysms were treated with bare platinum coils and who subsequently developed significant brain stem edema and hydrocephalus. They underlined that adverse inflammatory reactions to coiling of aneurysms are not limited to bioactive or hydrogel coils [29]. Complication rates among patients treated with HES in our study are slightly lower than described by other authors [23,24]. This may be due to the fact that we treated only unruptured aneurysms and we did not observe any complications that could be the result of intracranial bleeding.

All participants of our study underwent 12-month follow-up angiography, which demonstrated recanalization in 17.7% of all aneurysms. The type of coil used during the treatment did not affect the recurrence rate (HES – 18.0%, BPC – 17.4%, p = 0.9712). On the contrary, Fanning et al. reported significantly fewer major recurrences in the group treated with HES compared to the treatment with bare platinum coils (9.5% vs. 22.6%, p = 0.04). However, these were the results from intermediate follow-up angiograms (median 7.5 months) [24]. Gaba et al., in their study with follow-up angiography at average 12.3 months, also presented lower recurrence rate for the treatment with HES (17% vs. 24%) [23]. The HELPS trial, a controlled randomized clinical trial with 499 patients’ enrollment, demonstrated that there was a statistical difference in major recurrence and lower retreatment rates in the HES arm. The paper also demonstrated that the coil length was lower but a higher packing density 65% vs. 23% in the platinum arm [30]. According to the literature, the size of the aneurysms is a crucial factor for the success of endovascular coiling [4]. Our findings confirmed that there was a statistically significant difference in the aneurysm size between completely occluded aneurysms and aneurysms with residual flow. It was demonstrated in both immediate angiographic outcomes and long-term follow-ups. Deshaie et al. in their study of 67 aneurysms treated with HES reported a 3.7% recurrence rate for small aneurysm (≤7 mm) and a combined recurrence rate of 6% for small and large (8–15 mm) aneurysms. However, the results of treatment of very large (16–24 mm) and giant aneurysms (>25 mm) with that system were not so successful. Overall, one-year recurrence rate independent from size was estimated at 15% [27]. The limitation of our study was that we have not divided the treated aneurysms into the size categories, but the overall one-year recurrence rate observed by Deshaie et al. is similar to ours.

Gaba et al. reported a greater cost of HydroCoil in comparison with bare platinum coils in every aneurysm size category [23]. HES are 20% more expensive than BPS in our centre, and because of the increase in price and similar procedural outcomes, we do not use the HydroCoil routinely in our daily practice.

New generation of hydrogel coated coils have appeared on the market. In their recent study, Lee et al. compared 430 intracranial aneurysms treated with HydroSoft (MicroVention, Aliso Viejo, CA) coils with 252 aneurysms treated with bare platinum coils. Although they observed no difference between two types of coils in terms of initial angiographic outcomes they noted significantly reduced retreatment rate of coiled aneurysms at 12-month follow-up while using HydroSoft (adjusted RR, 0.21; 95% CI, 0.07–0.64; p = 0.004). They also showed that the use of HydroSoft as an embolic agent allows to achieve higher mean volumetric packing density (36.0 ± 8.5% vs. 31.1 ± 8.22%, p < 0.001) [31].

In comparison to the HELPS trial, the limitation of our study is a small number of patients. However, we treated unruptured aneurysms exclusively. Furthermore, there was no independent core lab associated with our study. Immediate and follow-up imaging was individually evaluated by the treating physician. It may account for the higher number of complete occlusions noted in comparison with other studies.

5. Conclusions

The risk of aneurysm recurrence is mainly defined by the size of aneurysm and the width of aneurysm neck which was a predictive factor in our series. Although, the use of the HES compared to the bare platinum coils tends to improve immediate angiographic outcome as demonstrated in the current publication (84.0% vs. 76.1%) there was no significant difference in the mid-term results (82.0% vs. 82.6%). In the HES arm, it also required less total number of coils to provide dense aneurysm filling. As with other similar publications, it appears that the HES is equivocal to bare platinum coils.

Conflict of interest

The authors declare that they have no conflict of interest. Competing interests THB is an employee of MicroVention/Terumo.

Ethical approval

All human and animal studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All persons gave their informed consent prior to their inclusion in the study.

References

[2] Debrun GM, Aletich VA, Kehrl T, Misra M, Ausman JI, Charbel F. Selection of cerebral aneurysms for treatment using Guglielmi detachable...


