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ORIGINAL RESEARCH

HydroCoil for Endovascular Aneurysm Occlusion (HEAL) Study: 3–6 Month Angiographic Follow-Up Results

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BACKGROUND AND PURPOSE: The HydroCoil Embolic System (HES) was developed reduce recurrences of aneurysms relative to platinum coils. This study was conducted to evaluate the recurrence rate of cerebral aneurysms 3–6 months after treatment with HES.

METHODS: We report the results in 135 cerebral aneurysms treated with HES in a prospective multicenter registry. Angiographic results 3–6 months after treatment were evaluated at a core laboratory. Wide variation in HES utilization within the HydroCoil for Endovascular Aneurysm Occlusion (HEAL) registry (HES representing 5% to 100% of the coil length used) allowed for subgroup analysis with regard to percentage length, last coil used, and packing attenuation in small (<10 mm) aneurysms.

RESULTS: The overall recurrence rate was 38 (28.1%) of 135, which included a number of large, giant, and previously recurrent aneurysms. When HES represented ≥75% of coil length, the recurrence rate was 0 (0%) of 18, whereas with <75% length of HES, the recurrence rate was 16 (23%) of 71 ($P = .035$). When the final coil deposited was a HES coil, the recurrence rate was 6 (11%) of 53, whereas when the final coil was platinum, the recurrence rate was 10 (29%) of 34 ($P = .047$). When the packing attenuation was ≥50%, the recurrence rate was 11 (19%) of 59, whereas for packing attenuation <50%, the recurrence rate was 5 (18%) of 28. The packing attenuation calculations were very error-prone.

CONCLUSION: Although the overall recurrence rates for small and large aneurysms in HEAL were no lower than published rates for aneurysms treated with platinum coils, patients treated in HEAL had a reduced recurrence rate when greater than 75% of the coil length used to treat an aneurysm was HES and when the final coil was HES.

A principal disadvantage of endovascular therapy of cerebral aneurysms with endovascular coils compared with surgical clipping is aneurysm recurrence.[1-3] An embolic agent that improves packing attenuation might reduce the rate of aneurysm recurrence.[4-7] The HydroCoil Embolic System (HES) (MicroVention, Aliso Viejo, Calif) was designed to improve packing attenuation/volumetric filling with an expansile hydrogel that should fill more of the aneurysm lumen than standard platinum coils,[8,9] improve aneurysm stability and durability, and provide a scaffold to initiate neointima formation and healing.[8,10] The HES is constructed as a hybrid hydrogel-platinum coil device (Fig 1). Early experience demonstrated that the HES allows substantially improved packing of the aneurysm lumen relative to standard platinum coils (72% versus 32%).[11]

The HEAL registry is a prospective registry of patients with cerebral aneurysms treated with the HES; the registry has shown that HES provides initial treatment success and complication rates comparable with those reported for platinum coils.[12] We report the 3–6-month angiographic follow-up results of cerebral aneurysms treated with the HES in the HEAL registry.

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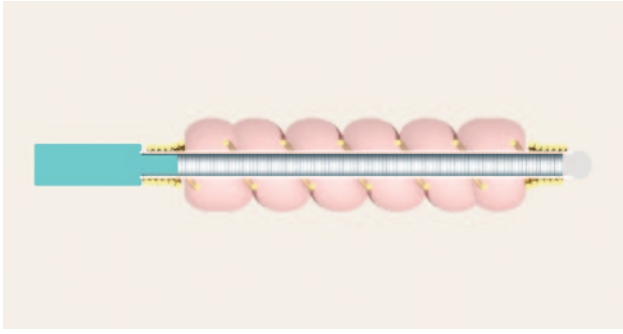

Fig 1. Schematic diagram of hybrid hydrogel-platinum coil device. *White*, primary platinum coil; *yellow*, platinum "overcoil"; *pink*, hydrogel; *teal*, delivery pusher.

Methods

The HEAL registry is a nonrandomized, multicenter, prospective study to investigate the safety and effectiveness of HES in patients with intracranial aneurysms deemed appropriate for endovascular treatment. A total of 15 sites in Europe and the United States participated in the investigation. The study was approved by each participating center's Institutional Review Board (IRB)/Ethics Committee. Written informed consent was obtained for each patient enrolled in the study. The total patient enrollment for the investigation was 184 patients with 191 aneurysms. Physician training and patient enrollment criteria have been described previously.[12]

Embolization Procedure. One or more platinum coils were generally used to establish the initial framework in the treatment of the aneurysm. The HES coils were generally used to provide additional filling of the aneurysm once the initial framework had been established by placement of 1 or more platinum complex coils. After place-

ment of the HES coils, additional platinum coils (eg, very soft platinum coils) were used at the discretion of the physician to complete the procedure. Angiograms were taken after the last coil was placed. In each case, the objective of the procedure was angiographic occlusion of the aneurysm.

Data Collection and Analysis. The following parameters were evaluated at the time of initial therapy with HES: aneurysm location; aneurysm size; aneurysm rupture status; number, type, and size of coils used in the procedure; degree of aneurysm occlusion postprocedure; and complications/adverse events.

A single interventional neuroradiologist (H.J.C.) with 8 years of experience with endovascular aneurysm therapy was the central reader who evaluated all of the angiograms. To prevent bias, the central reader did not participate as a treating physician in the study. The core laboratory conducted an analysis of the pretreatment and posttreatment angiograms, including the degree of aneurysm occlusion. The degree of aneurysm occlusion was classified as complete, nearly complete (≥95%), or incomplete (<95%). The core laboratory assessed the occlusion status of each aneurysm. The initial occlusion status was scored as either complete, nearly complete, or incomplete.

The aneurysm volume was calculated by assuming that the aneurysms were elliptical, using the formula: Aneurysm volume = 4 π(height/2 × length/2 × width/2)/3. Coil volumes were calculated by the formula: Coil volume = π (radius)^2 × length. The coil packing attenuation was expressed using the following formula: Packing attenuation = (coil volume/aneurysm volume) × 100%. Finally, the percentage length of HES used was calculated with the following formula: Percentage length HES = (length of HES/length of all coils) × 100%.

Two follow-up angiographic examinations are required in this investigation. Angiographic examinations were conducted at 3–6 months after the procedure. The core laboratory conducted an analysis of the follow-up angiograms, including the degree of aneurysm occlusion, coil compaction, recanalization, and parent artery patency. Comparisons were made with the initial posttreatment angiograms. The core laboratory recorded the occlusion status of the aneurysm. The occlusion status was scored as either complete, nearly complete, or incomplete. The occlusion status at 3–6 months was also classified as better, same, or worse than the initial postprocedure angiogram.

The hypothesis of the investigation was that the recanalization rate for the treatment group will be equal to or better than the published rates for aneurysms treated with platinum coils. Because operating physicians had a lot of freedom with regard to proportions of HES and platinum coils used, there was a rather wide variation in the choice of coils. This allowed for comparisons of recurrence rates to be made between subgroups with regard to the operators choices of coils. Subgroup analysis was performed to evaluate the effect of packing attenuation, percentage length of HES, and last coil used on recurrence rate. Recurrence rates in aneurysms treated with a packing attenuations of ≥50% and <50% were compared. Recurrence rates in aneurysms treated with percentage lengths of HES of ≥75% and <75% were compared. Recurrence rates in aneurysms treated with HES or platinum as the final coil were compared. Recurrence rates for subgroups were evaluated for statistical significance using a 2-tailed Fisher exact test. A P value of ≤.05 was considered statistically significant.

Results

Aneurysms Treated. Angiographic follow-up at 3–6 months after endovascular therapy was obtained in 135 of 191 aneurysms treated. Aneurysms included were located in a wide variety of locations in both the anterior and posterior circulation. The mean aneurysm size was 8.2 mm, and the median was 6.5 mm. The mean neck diameter was 5.4 mm, and the median was 4.4 mm. The mean dome-to-neck ratio was 2.0, and the median was 1.7. There were 46 ruptured aneurysms (34%) and 89 unruptured aneurysms (63%). Balloon remodeling was used in 9 cases, and adjunctive stent placement was used in 5 cases. Thirteen aneurysms had been previously treated with platinum coils and thus were recurrences that were being treated with HES.

Recurrence rates for aneurysms treated in HEAL registry

	Recurrence Rates	
	Minor	Major
All aneurysms	8.9% (12/135)	19.2% (26/135)
Small aneurysms	10.3% (9/87)	8.0% (7/87)
Large aneurysms	3.3% (1/30)	43.3% (13/30)
Giant aneurysms	0.0% (0/5)	80.0% (4/5)
Previously treated aneurysms	15.4% (2/13)	15.4% (2/13)

Note:—HEAL indicates HydroCoil for Endovascular Aneurysm Occlusion.

Coils Used. The mean number of HES coils per case was 5.1, and the median was 3.0. The mean number of platinum coils was 3.5, and the median was 3.0. The HES provided a relatively high packing attenuation, with a mean of 45% and a median of 44%. The mean percentage length of HES used was 40%, and the median was 46%. The range of percentage length of HES was 5%–100%.

Recurrence Rates. The overall recurrence rates are shown in the Table. For small aneurysms (<10 mm), enough data were available for subgroup analysis. When HES represented ≥75% of coil length in an aneurysm, the recurrence rate was 0 (0%) of 18, whereas for aneurysms with <75% length HES, the recurrence rate was 16 (23%) of 71 (P = .035). When the final coil deposited was an HES coil, the recurrence rate was 6 (11%) of 53, whereas when the final coil was platinum, the recurrence rate was 10 (29%) of 34 (P = .047). Recurrence rate did not correlate with packing attenuation. When the packing attenuation was ≥50%, the recurrence rate was 11 (19%) of 59, whereas for aneurysm with packing attenuation <50%, the recurrence rate was 5 (18%) of 28. Because the packing attenuation was calculated based on assessments of aneurysm volume calculated from linear aneurysm measurements made from films from a variety of medical centers, they are prone to significant error.

Discussion

The overall recurrence rates for small and large aneurysms treated in HEAL were not lower than what has been reported for aneurysms treated with platinum coils.[13] However, the variety of coil combinations used by the physicians in HEAL created a natural experiment that allowed for subgroup analysis that uncovered promising trends. A relative reduction in recurrence rate was noted in aneurysms treated with percentage length of HES greater than 75%, as well as when the final coil was an HES coil. Because both an increase in percentage length of HES and the use of HES as the final coil can be expected to correlate with an increase in HES loops at the aneurysm neck, a reduction in recurrence related to these factors may reflect a biologic effect of HES at the neck of the aneurysms. Having a higher overall proportion of HES coils relative to the total length of coils in an aneurysm (ie, percent-

age length of HES) increases the proportion of loops covered with hydrogel everywhere in the aneurysm, including at the neck. Although it cannot be known with certainty where the final coil in each case was deposited, it is reasonable to assume that, in most cases, the final coil was deposited near the neck of the aneurysm. Thus, aneurysms treated with HES as the final coil are more likely to have more hydrogel deposited at the neck of the aneurysm than aneurysms treated with a platinum coil as the final coil. A reaction of hydrogel with tissue at the aneurysm neck might promote a healing reaction that diminishes aneurysm recurrence.[10]

We did not find correlation between packing attenuation and recurrence rate, but there is much error in the calculation of packing attenuation based on linear measurements in the HEAL study. The HES provides a mean packing attenuation that is higher than is achievable with platinum coils.[11,12,14] The packing attenuation for individual cases is greatly error-prone because the assessment of volumes of aneurysms is error-prone. The volumes of aneurysms determined in HEAL are subject to much error because precise size measurements cannot accurately be determined based on 2-dimensional angiographic images from multiple medical centers that use various angiographic equipment and because aneurysms often have irregular shapes that do not allow for simple volume calculations. In addition, the packing attenuation calculation assumes complete expansion of the hydrogel, which may not be possible if the hydrogel is constrained by adjacent coil loops. Our finding of no relationship between packing attenuation and recurrence rate may be because packing attenuation is less important to altering recurrence rate than tissue reaction to hydrogel at the neck of the aneurysm.

The HES was generally not the only type of coil used to treat aneurysms in the HEAL registry; ie, platinum coils were generally used together with HES. Platinum coils were usually used to form a "basket" or "framework" for subsequent deposition of HES 14 coils. The HES 14 coils were then used to fill most of the aneurysm volume. The HES 14 coil is stiffer than standard platinum coils, and therefore it is often not generally used as the final, or "finishing" coil. Rather, the final coil was often a small, soft platinum coil. Smaller and softer HES 10 coils suitable for use as "finishing" coils are now available that allow for improved packing of aneurysms with hydrogel, as well as increased deposition of HES at the neck of the aneurysm.

For patients enrolled in HEAL, follow-up angiography is also being performed at 12–18 months. These later follow-up data are still being collected. A second version of the HEAL study, HEAL2, has been designed to further test the findings of HEAL. HEAL2 provides more specific operator instructions, designed to increase the percentage length of HES used, and to encourage the deposition of HES at the neck of the aneurysm. Patient enrollment for HEAL2 has already begun. In addition, a prospective, randomized, controlled trial comparing durability of cerebral aneurysm treatment with platinum coils versus HES is currently being conducted (HydroCoil: Endovascular Aneurysm Occlusion and Packing Study [HELPS]).

Conclusion

The overall recurrence rates for small and large aneurysms in HEAL were no lower than published rates for aneurysms treated with platinum coils. However, there was a wide variation in utilization of HES within the HEAL registry; HES represented 5%–100% of the coil length used in any given aneurysm. Patients treated in HEAL had a reduced recurrence rate when greater than 75% of the coil length used to treat an aneurysm was HES and when the final coil was HES. The HES represents a new technology that potentially can offer improved outcomes relative to platinum coils.

Appendix

Core Laboratory, Data Analysis, and Manuscript Preparation

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Principal Investigators at Enrolling Sites

Timothy Malisch, University of Illinois at Chicago; Alejandro Berenstein, Beth Israel Hospital; Emmanual Houdart, Hopital Lariboisier; Isabel Wanke, Universitatsklinik Essen; In Sup Choi, Lahey Clinic; Harish Shownkeen, Loyola University Hospital; Laurent Pierot, Centre Hospitalier Universitaire de Reims; Frank Tong, Emory University Hospital; Soren Bakke, Rikshospitalet; Beverly Aagaard, University of Wisconsin Hospital; Jacques Moret, Foundation Rothschild; Serge Bracard, Centre Hospitaler Universitaire de Nancy; Avery Evans, Tampa General Hospital; Mary Jensen, University of Virginia; Hans Henkes, Alfred Krupp Krankenhaus.

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