Original Article

Ewha Med J 2012;35(1):38-43
pISSN 2234-3180 / eISSN 2234-2591

EMJ
THE EWHA MEDICAL JOURNAL

Endovascular Treatment of Intracranial Aneurysms Using Polymer Polyglycolic-Lactic Acid Coated Coils

Sung-Kyun Hwang, Sung-Hak Kim

Department of Neurosurgery, Ewha Womans University School of Medicine, Seoul, Korea

Objectives: In treatment for intracranial aneurysms by coil embolization, recanalization remains the major limitation of coiling, particularly wide-necked or larger aneurysms. The aim of this study was to evaluate technical results and clinical outcome in a single center of consecutive patients with intracranial aneurysms treated with endovascular embolization using polyglycolic-lactic acid (PGLA) coated coils.
Methods: Between January 2005 and December 2010, 33 patients (male, 8 patients; female, 25 patients; mean age, 57 years) with saccular intracranial aneurysms were treated by means of an endovascular approach using PGLA coated coils. The endovascular procedures and technical outcomes were evaluated. The mean follow-up duration was 15.9 months (range, 6 to 72 months).
Results: Successful embolizations with satisfactory results were achieved in 91%. The degree of occlusion of the treated aneurysm was complete in 23 (69.6%), small neck remnant in 7 (21.2%), and residual filling in 3 (9%). Thirty patients (90.9%) showed no interval change of the residual neck. Three patients (9.1%) demonstrated the recanalization, and 2 of them were successfully recoiled.
Conclusion: This preliminary study showed that PGLA coated coils may be safe option and preventable for recanalization in patients with intracranial aneurysms. Further study with more cases, longer follow-up data and well controlled design are required to confirm our results. **(Ewha Med J 2012;35(1):38-43)**

Key Words: Endovascular treatment; Intracranial aneurysm; Polyglycolic-lactic acid coated coil

Introduction

Recanalization of cerebral aneurysms after coiling remains a problem. Endovascular coiling of intracranial aneurysms has been progressively more accepted worldwide. However, recanalization attributable to coil compaction remains the major limitation of coiling, particularly wide-necked or larger aneurysms. Mid- and long-term clinical outcome and follow-up angiographic findings confirm that recanalization may occur up to 30%, which also tends to increase in the aneurysms [1-12].

Several histological studies [2,13-17] have demonstrated that platinum coils induce thrombus formation within the aneurysm sac shortly after treatment. Fresh thrombus, however, is unstable and subject to thrombolysis. Organization of thrombus into granulation tissue is thought to be necessary for healing to be completed. In many cases, however, thrombus organization occurs very late and may remain incomplete in the long term. To develop better devices for embolization that would induce a healing reaction, different materials have been applied experimentally either in-

Received: January 9, 2012, Accepted: February 19, 2012

Corresponding author: Sung-Kyun Hwang, Department of Neurosurgery, Ewha Womans University School of Medicine, 1071 Anyangcheon-ro, Yangcheon-gu, Seoul 158-710, Korea
Tel: 82-2-2650-2872, Fax: 82-2-2650-0948
E-mail: nshsg@ewha.ac.kr

side or on the surface of platinum microcoils, including collagen, tissue plasminogen activator inhibitor and tissue thromboplastin, and vitronectin, laminin, fibrinogen, and fibronectin.

Coils coated with a resorbable polyglycolic lactic acid (PGLA) polymer are believed to accelerate intra-aneurysmal thrombus organization and aneurysm fibrosis. As an initial neck remnant may be the cause of inferior delayed angiographic and clinical outcomes, we hypothesized that PGLA-coated coils could lead to progressive occlusion of the neck remnant and to better angiographic results during follow-up [18-30].

This study aimed to evaluate the effects of the bioactive PGLA-coated coils regarding the durability of endovascular coiling and the efficacy at preventing recanalization. We present our clinical experience with this system providing follow-up data.

Methods

1. Patients

A series of consecutive 33 patients harboring an intracranial aneurysm were treated at our institutions via the endovascular approach using PGLA-coated coils (Matrix coil, Boston Scientific, Freemont, CA, USA) between January 2005 and December 2010. All patients underwent conventional angiography of both carotid arteries. The selection criteria for this study were: 1) spontaneous subarachnoid hemorrhage (aneurysm rupture as the cause of subarachnoid hemorrhage) or unruptured aneurysms between January 2005 and December 2010, 2) endovascular aneurysm treatment chosen as the first line of treatment, 3) that aneurysm repair treatment was given at the acute stage after hemorrhage (within 3 weeks of aneurysm rupture), and 4) patients with fusiform, traumatic, or mycotic aneurysm were excluded from the study. In this series, 25 were females (75.7%) and 8 (24.2%) were males. The patients' ages ranged from 22 to 77 years, with an average age of 57 years.

2. Aneurysm characteristics

Regarding the aneurysm size, 2 lesions (6%) were small (<3 mm in diameter), 30 lesions (90.9%) were medium (3~15 mm in diameter), and 1 lesion (3%) was large (15~25 mm in diameter). Regarding the aneurysm neck size, 29 lesions (87.8%) had a small neck (≤4 mm), whereas 4 lesions (12.1%) had a wide neck (>4 mm).

3. Clinical presentation

Four unruptured aneurysms (12.1%) were incidental, and twenty-nine (87.8%) presented with a subarachnoid hemorrhage. Of these, one patient (3%) was categorized in Hunt and Hess grade I, 20 (60.6%) in grade II, 7 (21.2%) in grade III, and 1 (3%) in grade IV.

4. Follow-up and outcome

After embolization, all patients were followed up by plain skull image, at least one time every 1 or 2 months schedule according to patient's conditions.

5. Endovascular embolization procedure

Coiling of aneurysms was performed on a biplane angiographic unit (Integris BN 3000, Phillips Medical Systems, Eindhoven, Netherland). Embolization was performed after induction of general anesthesia and systemic heparinization (3,000 IU bolus, followed by continuous intra-arterial infusion of heparin at 1,000 IU/hour) and maintenance of an activated coagulation time to twice the control value. After road mapping, a microcatheter (Excelsior SL-10, Boston Scientific, Boston, USA; Prowler 14, Cordis, Miami, FL, USA) with appropriate tip shape was carefully inserted into the aneurysm over the guidewire, and coils were then introduced. Aneurysms were embolized using PGLA coated coils (Matrix coils, Boston Scientific, Boston, MA, USA). The aim of coiling was obtainment an attenuated packing of the aneurysm, until not a single coil could be placed.

Results

1. Treatment results

A complete aneurysm occlusion was attained in 23 cases (69.6%). A neck remnant was detected in 7 cases (21.2%), and in 3 (9%) a residual filling of a portion of the aneurysm was observed. Satisfactory occlusion

rate (complete occlusion or neck remnant) was achieved in 91% of patients.

2. Follow-up and outcome

In 33 cases at least one plain skull image follow-up study was performed. In 30 cases (90.9%) no change in the degree of coil shape was detected. One case with wide-necked subtotally occluded aneurysms after the procedure, the plain skull image and angiogram showed compaction of the coils into the aneurysm (recanalization): 2 cases of these cases required a second embolization session.

Discussion

Incomplete aneurysm occlusion, persistent neck remnant, regrowth, and recanalization are frequently associated with endosaccular packing of both ruptured and unruptured aneurysm. The long-term follow-up results of previous trial clearly documented the higher incidence of aneurysm recurrence and subsequent late re-treatment rate after primary endovascular coiling [1,3-10,12,31,32]. The study conducted by Raymond et al. [9] evaluating 383 aneurysms, reported a recanalization rate of 33.6% and retreatment rate of 20.7%. In that study, the residual aneurysm filling at initial treatment and the aneurysm size (>10 mm) were identified as the most significant predictors of recurrence, whereas neck size >4 mm, acute rupture, residual neck, and length of follow-up period showed less impact on recurrence rate.

The exact mechanism by which, thrombosis and formation of neointimal proliferation after coil embolization is not known. Platinum coils elicit a mild biological response when deployed into an aneurysm. From histopathological reports on human aneurysm embolized with coils, it appears that the intra-aneurysmal clot undergoes a slow organization [17,24]. Therefore, when such phenomenon do not occur, the effect of pulsatile blood flow against inert platinum causes the coil mass to compact, leading to eventual aneurysmal recanalization. For all these reasons, investigators have explored the use of coils that promote organization of the initial thrombus such as polymercoated coils [2,13-17].

With regard to polymer-coated coils, it has been reported that aneurysm thrombosis could be controlled by the composition of the polymer ratio. This means that even in a "tightly packed" aneurysm, 75% of the aneurysm sac is filled with thrombus. Fresh, unorganized thrombus is unstable, because it is subject to fibrinolysis. Fibrotic transformation of the thrombus is necessary for the intra-aneurysmal mass to become a permanent barrier that resists both the mechanical effect of pulsatile blood flow and the fibrinolytic mechanisms [7]. Histologically, bioabsorbable polymer was replaced by mature connective tissue. These coils are intended to deliver a biochemical agent within the aneurysm cavity, which is supposed to accelerate thrombus organization into fibrocellular granulation tissue.

Recently, new bioactive Matrix coils (Boston Scientific, Freemont, CA, USA) and Cerecyte coils (Micrus Endovascular, San Jose, CA, USA) incorporated with a surgical suture material have been introduced into clinical use. They aim to increase the long-term efficacy of endovascular coiling by improved packing density and/ or better neointima formation at the neck of the aneurysm. However, the series with Matrix coils resulted in worse recanalization rate than that reported for Guglielmi detachable bare platinum coils [20]. Niimi et al. [33] reported an overall recanalization rate of 57.4% in the group of aneurysm with follow-up. In the subgroup of aneurysms (46 aneurysms), which were embolized by Matrix coils consisting of >50% of coil length, recanalization rate was 54.3%. Fiorella et al. [20] reported their series of 131 aneurysms treated with Matrix coils with a mean follow-up interval of 6.9 months. Of the entire series, 82 aneurysms had follow-up data with an overall 36.6% recanalization rate and 23.1% re-treatment rate.

The bioactive coating of PGLA coil (Matrix coil) is reportedly absorbed in 3 months. Most of recanalized cases were recognized on the first follow-up angiogram within 1 year of treatment, some of which showed progression of recanalization on the second follow-up angiogram. The main cause of the poor initial results is most likely the high friction of PGLA coil, which causes compartmentalization of the coils within the aneurysm, preventing dense packing. Friction is prob-

ably related to the high amount of polymer (70%) supported by a small central wire (30%) as designed in the first generation PGLA coil. It was hypothesized that the high percentage of polymer creates an increase in contact points between the coil and the inner surface of the catheter. Consequently, the axial force required to advance the coil is higher. With regard to compartmentalization, the polymer is braided over the wire, therefore not allowing break points within the coil to be active. This may result in less compliance of the coil as it folds against the endothelium of the aneurysm and other coils. Another possible cause of the high recanalization rate of PGLA coil demonstrated in may be the absorbable nature of the bioactive coating. The bioactive coating of the PGLA coil, which comprises 70% by volume, is absorbed in 3 months. If complete aneurysm closure does not occur by this time, the amount by volume of platinum within the aneurysm may ultimately only be 10% or less, which may not be enough to prevent recanalization mechanically [5-7,16,17,20,27-29].

PGLA coated coils have not yet been compared in large, randomized, prospective, long-term studies. Pierot et al. [26] achieved complete initial occlusion in 44% of the cases coiled with PGLA coated coils alone or combined with platinum coils. However, they had no control group and did not yet assess durability. Niimi et al. [33] made a follow-up for an average of 12 months of 47 aneurysms embolized with PGLA coated coils, during which time recanalization rate was 57.4%, which is worse than reported for platinum coils. In their 8 months follow-up of 87 patients, Murayama et al. [7] found the number of aneurysms coiled with PGLA coils remaining stable or exhibiting progressive occlusion to be 80.5%. Moreover, no recanalization appeared in aneurysms that were initially completely occluded. Some aneurysms with a neck remnant showed progressive occlusion, similar to our results in rats. The results of our study were similar or better to those reported by other investigator clinically.

However, we acknowledge that this study has several weak points. 1) The total number of aneurysms is small. There can be a sample selection bias. 2) Follow-up data of the shorter period was available in the PGLA coils group. Not all patients have long-term angiographic follow-up. The smaller number of cases in the group underwent conventional angiography in light of our follow-up protocol. 3) The study does not contain a control group with coil embolization procedure alone. 4) A comparison with clinical data on patients treated with new PGLA coils is not yet available.

Recent knowledge is now growing regarding aneurysm pathobiology and the ongoing technical development of coils should emphasize on the biologic effects. In the future, biologically active coils may work in such a way that even incompletely coiled aneurysms would progressively and completely occlude. Further study with more cases, longer follow-up data and well controlled design are required to ascertain our results.

References

1. Butteriss D, Gholkar A, Mitra D, Birchall D, Jayakrishnan V. Single-center experience of cerecyte coils in the treatment of intracranial aneurysms: initial experience and early follow-up results. *AJNR Am J Neuroradiol* 2008;29:53-56.
2. Ding YH, Dai D, Lewis DA, Cloft HJ, Kallmes DF. Angiographic and histologic analysis of experimental aneurysms embolized with platinum coils, Matrix, and HydroCoil. *AJNR Am J Neuroradiol* 2005;26:1757-1763.
3. Gaba RC, Ansari SA, Roy SS, Marden FA, Viana MA, Malisch TW. Embolization of intracranial aneurysms with hydrogel-coated coils versus inert platinum coils: effects on packing density, coil length and quantity, procedure performance, cost, length of hospital stay, and durability of therapy. *Stroke* 2006;37:1443-1450.
4. Geyik S, Yavuz K, Cekirge S, Saatci I. Endovascular treatment of basilar and ICA termination aneurysms: effects of the use of HydroCoils on treatment stability in a subgroup of patients prone to a higher recurrence rate. *Neuroradiology* 2007;49:1015-1021.
5. Ishii A, Murayama Y, Nien YL, Yuki I, Adapon PH, Kim R, et al. Immediate and midterm outcomes of patients with cerebral aneurysms treated with Matrix1 and Matrix2 coils: a comparative analysis based on a single-center experience in 250 consecutive cases. *Neurosurgery* 2008;63:1071-1077.
6. Kang HS, Han MH, Kwon BJ, Kwon OK, Kim SH, Choi SH, et al. Short-term outcome of intracranial aneurysms treated with polyglycolic acid/lactide copolymer-coated coils compared to historical controls treated with bare

platinum coils: a single-center experience. *AJNR Am J Neuroradiol* 2005;26:1921-1928.
7. Murayama Y, Vinuela F, Ishii A, Nien YL, Yuki I, Duckwiler G, et al. Initial clinical experience with matrix detachable coils for the treatment of intracranial aneurysms. *J Neurosurg* 2006;105:192-199.
8. Piotin M, Spelle L, Mounayer C, Salles-Rezende MT, Giansante-Abud D, Vanzin-Santos R, et al. Intracranial aneurysms: treatment with bare platinum coils--aneurysm packing, complex coils, and angiographic recurrence. *Radiology* 2007;243:500-508.
9. Raymond J, Roy D, Leblanc P, Roorda S, Janicki C, Normandeau L, et al. Endovascular treatment of intracranial aneurysms with radioactive coils: initial clinical experience. *Stroke* 2003;34:2801-2806.
10. Veznedaroglu E, Koebbe CJ, Siddiqui A, Rosenwasser RH. Initial experience with bioactive cerecyte detachable coils: impact on reducing recurrence rates. *Neurosurgery* 2008;62:799-805.
11. Wong GK, Poon WS. Thromboembolic complications of endovascular aneurysm occlusion using matrix detachable coils. *Stroke* 2006;37:1363.
12. Wong GK, Yu SC, Poon WS. Clinical and angiographic outcome of intracranial aneurysms treated with Matrix detachable coils in Chinese patients. *Surg Neurol* 2007; 67:122-126.
13. Ding YH, Dai D, Kadirvel R, Lewis DA, Cloft HJ, Kallmes DF. Relationship between aneurysm volume and histologic healing after coil embolization in elastase-induced aneurysms: a retrospective study. *AJNR Am J Neuroradiol* 2008;29:98-101.
14. Kadirvel R, Dai D, Ding YH, Danielson MA, Lewis DA, Cloft HJ, et al. Endovascular treatment of aneurysms: healing mechanisms in a Swine model are associated with increased expression of matrix metalloproteinases, vascular cell adhesion molecule-1, and vascular endothelial growth factor, and decreased expression of tissue inhibitors of matrix metalloproteinases. *AJNR Am J Neuroradiol* 2007;28:849-856.
15. Killer M, Hauser T, Wenger A, Richling B, Ladurner G. Comparison of experimental aneurysms embolized with second-generation embolic devices and platinum coils. *Acta Neurochir (Wien)* 2009;151:497-505.
16. Marjamaa J, Tulamo R, Frösen J, Abo-Ramadan U, Hernesniemi JA, Niemelä MR, et al. Occlusion of neck remnant in experimental rat aneurysms after treatment with platinum- or polyglycolic-polylactic acid-coated coils. *Surg Neurol* 2009;71:458-465.
17. Szikora I, Seifert P, Hanzely Z, Kulcsar Z, Berentei Z, Marosfoi M, et al. Histopathologic evaluation of aneurysms treated with Guglielmi detachable coils or matrix detachable microcoils. *AJNR Am J Neuroradiol* 2006;27:283-288.
18. Bendszus M, Solymosi L. Cerecyte coils in the treatment of intracranial aneurysms: a preliminary clinical study. *AJNR Am J Neuroradiol* 2006;27:2053-2057.
19. Castro E, Villoria F, Castaño C, Romance A, Mendez JC, Barrena R, et al. Spanish registry for embolization of small intracranial aneurysms with cerecyte coils (SPAREC) study: early experience and mid-term follow-up results. *Interv Neuroradiol* 2008;14:375-384.
20. Fiorella D, Albuquerque FC, McDougall CG. Durability of aneurysm embolization with matrix detachable coils. *Neurosurgery* 2006;58:51-59.
21. Geyik S, Ertugrul O, Yavuz K, Geyik P, Saatci I, Cekirge HS. Comparison of bioactive coils and bare platinum coils for treatment of intracranial aneurysms: a matched-pair analysis. *J Neurosurg* 2010;112:709-713.
22. Geyik S, Yavuz K, Ergun O, Koc O, Cekirge S, Saatci I. Endovascular treatment of intracranial aneurysms with bioactive Cerecyte coils: effects on treatment stability. *Neuroradiology* 2008;50:787-793.
23. Leonardi M, Dall'olio M, Vasquez OO, Quercetti C. Preliminary experience of cerecyte coils in the treatment of intracranial aneurysms. *Interv Neuroradiol* 2008;14: 285-292.
24. Linfante I, Akkawi NM, Perlow A, Andreone V, Wakhloo AK. Polyglycolide/polylactide-coated platinum coils for patients with ruptured and unruptured cerebral aneurysms: a single-center experience. *Stroke* 2005;36:1948-1953.
25. Linfante I, DeLeo MJ 3rd, Gounis MJ, Brooks CS, Wakhloo AK. Cerecyte versus platinum coils in the treatment of intracranial aneurysms: packing attenuation and clinical and angiographic midterm results. *AJNR Am J Neuroradiol* 2009;30:1496-1501.
26. Pierot L, Bonafe A, Bracard S, Leclerc X; French Matrix Registry Investigators. Endovascular treatment of intracranial aneurysms with matrix detachable coils: immediate posttreatment results from a prospective multicenter registry. *AJNR Am J Neuroradiol* 2006;27:1693-1699.
27. Pierot L, Leclerc X, Bonafe A, Bracard S; French Matrix Registry Investigators. Endovascular treatment of intracranial aneurysms with matrix detachable coils: midterm anatomic follow-up from a prospective multicenter registry. *AJNR Am J Neuroradiol* 2008;29:57-61.
28. Pierot L, Leclerc X, Bonafe A, Bracard S; French Matrix Registry Investigators. Endovascular treatment of intracranial aneurysms using Matrix coils: short- and mid-term results in ruptured and unruptured aneurysms. *Neurosurgery* 2008;63:850-857.

29. Piotin M, Spelle L, Mounayer C, Loureiros C, Ghorbani A, Moret J. Intracranial aneurysms coiling with matrix: immediate results in 152 patients and midterm anatomic follow-up from 115 patients. *Stroke* 2009;40:321-323.
30. Turk AS, Luty CM, Carr-Brendel V, Polyakov I, Consigny D, Grinde J, et al. Angiographic and histological comparison of canine bifurcation aneurysms treated with first generation matrix and standard GDC coils. *Neuroradiology* 2008;50:57-65.
31. Fanning NF, Berentei Z, Brennan PR, Thornton J. HydroCoil as an adjuvant to bare platinum coil treatment of 100 cerebral aneurysms. *Neuroradiology* 2007; 49:139-148.
32. Sluzewski M, van Rooij WJ, Slob MJ, Bescos JO, Slump CH, Wijnalda D. Relation between aneurysm volume, packing, and compaction in 145 cerebral aneurysms treated with coils. *Radiology* 2004;231:653-658.
33. Niimi Y, Song J, Madrid M, Berenstein A. Endosaccular treatment of intracranial aneurysms using matrix coils: early experience and midterm follow-up. *Stroke* 2006;37: 1028-1032.