CLINICAL ARTICLE

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Angiographic Follow-up Result of Cerebral Aneurysms Treated with Coils Covered with Polyglycolic-Polylactic Acid Copolymer

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Objective : We evaluate the effect of the copolymer-coated coils on immediate occlusion of the aneurysm, preventing rupture, and decreasing compaction or re-growth.

Methods : Thirty-five aneurysms treated between September 2003 and December 2004 using Matrix detachable coil were reviewed. Study population consisted of 12 men and 23 women ranging in age from 34 to 75 years(mean, 55.1 years). Twenty-two aneurysms were ruptured and 23 aneurysms were located in the anterior circulation. Follow-up angiography was obtained in 16 patients after 6 months from the procedure.

Results : Initial complete occlusion was achieved in 17 aneurysms(48.6%), and the others remained as a residual neck in 8 aneurysms(22.8%) and residual sac in 10 aneurysms(28.6%). Among these incompletely occluded aneurysms, 7 aneurysms were performed follow-up angiography. And 6 of them converted into complete occlusion. In the other hands, among 17 aneurysms achieved complete occlusion initially, 9 aneurysms were performed follow-up angiography. Recurrence due to coil compaction occurred in one aneurysm and the others maintained complete occlusion. There was one mortality case due to thromboembolic complication.

Conclusion : In spite of difficulty in achieving complete occlusion with Matrix coil system, there is no rupture or re-rupture during follow-up period. Follow-up angiography shows many conversions of residual sac into complete occlusion. Embolization using Matrix coil system is safe and effective, but the effects of PGLA copolymer need further investigation.

KEY WORDS : Cerebral aneurysm · Embolization · Matrix · Co-polymer · polyglycolic-polylactic acid.

Introduction

Endovascular treatment of cerebral aneurysms is an effective alternative to surgical clipping. Detachable coils has been evolved repeatedly since it's first introduction in 1991, but criticism involving possibility of re-growth or re-canalization of coiled aneurysms requiring additional treatment, is still remained. Matrix detachable coil(Boston Scientific, Fremont, CA) is a platinum coil covered with absorbable copolymer. Polyglycolic-polylactic acid(PGLA) copolymer, consisting approximately 70% of the coil volume, accelerates aneurysm fibrosis and neointima formation[17].

On the other hand, if the coated copolymer absorbed without complete organization and fibrosis of the aneurysm, the smaller platinum core of Matrix coil may less resist blood flow. This may predispose re-growth of the aneurysm, re-canalization or compaction of the coils.

Currently, there is no clinical data concerning the effects of Matrix detachable coil on immediate occlusion of the aneurysm, preventing rupture, and decreasing compaction or re-growth. We have treated cerebral aneurysms with Matrix detachable coil from September, 2003 and analyzed immediate and 6 months follow-up angiographic results of cerebral aneurysms treated with this coil.

Materials and Methods

Between September 2003 and December 2004, we treated 51 patients with 53 aneurysms with Matrix coil system at our hospital. In the present study, we excluded following

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Table 1. Demographic presentation of the patients

		Total		Follow-Up	
Sex	(M:F)	12	23	6	10
Age	(Mean)	55.1	–	49.8	–
Location	–	–	–	–	–
Anterior	–	–	27	–	12
	ACoA	6	–	3	–
	PCoA	6	–	2	–
	Carotid Cave	5	–	5	–
	A2	4	–	0	–
	Paraclinoid	1	–	1	–
	SHP	1	–	0	–
	IB	2	–	0	–
	AChoA	2	–	1	–
Posterior	–	–	8	–	4
	BB	3	–	1	–
	SCA	2	–	0	–
	PICA	2	–	2	–
	AICA	1	–	1	–
Neuroform		7	–	5	–
Volume	(Mean, mm^3)	96.8	–	61.8	–
Packing	(Mean, %)	31.1	–	29.8	–
Result		–	–	–	– –
	Complete	19	–	7	No Change
	–	–	–	1	Compaction
	Residual Neck	10	–	1	No Change
	–	–	–	0	Compaction
	–	–	–	1	Complete
	Residual Sac	10	–	0	No Change
	–	–	–	0	Compaction
	–	–	–	5	Complete

ACoA : Anterior communicating artery, AChoA : Anterior choroidal artery, A2 : Second segment of anterior cerebral artery, AICA: Anterior inferior cerebellar artery, BB : Basilar bifurcation, IB : Bifurcation of internal carotid artery, PCoA, Posterior communicating artery, PICA : Posterior inferior cerebellar artery, SCA : Superior cerebellar artery, SHP : Superior hypophyseal artery

Table 2. Geometric analysis of the aneurysms

Factors		Immediage Results			Follow-Up Results	
		Mean	Range		Mean	Range
Mean Volume						
	Complete	101.38	(13.5~390.0)	–	57.20	(13.1~195.0)
	RN	112.67	(15.0~427.5)	–	78.80	*
	RS	30.28	(7.5~71.5)	–	–	–
		–	–	Compaction	24.50	*
Mean Packing		–	–	–	–	–
Ratio	Complete	33.34	(13.4~63.8)	–	27.67	(7.8~63.8)
	RN	31.69	(14.7~64.0)	–	28.90	*
	RS	30.28	(7.8~35.8)	–	–	–
		–	–	Compaction	48.20	*
D/N(L)	–	–	–	–	–	–
	Complete	1.27	(0.9~2.0)	–	1.18	(0.9~1.7)
	RN	1.30	(1.0~2.0)	–	1.80	*
	RS	1.27	(0.9~2.3)	–	–	–
		–	–	Compaction	1.00	*
D/N(W)	–	–	–	–	–	–
	Complete	1.55	(1.0~2.1)	–	1.31	(0.9~1.8)
	RN	1.54	(1.0~3.0)	–	1.70	*
	RS	1.31	(0.9~2.2)	–	–	–
		–	–	Compaction	1.00	*
D/H	–	–	–	–	–	–
	Complete	1.01	(0.5~1.8)	–	0.95	(0.5~1.4)
	RN	0.78	(0.4~1.6)	–	1.60	*
	RS	1.01	(0.6~1.4)	–	–	–
		–	–	Compaction	1.10	*
Neck(L)	–	–	–	–	–	–
	Complete	4.26	(2.0~7.5)	–	3.82	(2.5~5.0)
	RN	3.75	(2.0~5.5)	–	4.00	*
	RS	3.20	(1.5~5.0)	–	–	–
		–	–	Compaction	4.00	*
Neck(W)	–	–	–	–	–	–
	Complete	3.56	(2.0~5.5)	–	3.57	(2.5~5.0)
	RN	3.31	(2.0~6.0)	–	3.00	*
	RS	3.05	(2.0~4.0)	–	–	–
		–	–	Compaction	3.50	*

RN : Residual neck, RS : Residual sac, D/N : Dome-to-neck ratio, D/H : Dome-to-height ratio, L : Length(Along the parent artery), W : Width(Across the parent artery), * : Only one case

aneurysms; 1) recurrent aneurysms after clipping, wrapping or embolization, 2) suspected dissecting aneurysms or pseudoaneurysms, 3) tandem aneurysms, 4) giant aneurysm, 5) aneurysms arising from the feeding artery of the arteriovenous malformation, 6) combined use of Matrix coils with bare platinum coils, 7) planned partial treatment. Finally, we selected 35 aneurysms treated with matrix coils for the first time. Our study population consisted of 12 men and 23 women ranging in age from 34 to 75 years(mean, 55.1 years). Twenty-two aneurysms were ruptured, eleven aneurysms were asymptomatic aneurysm in multiple aneurysms in patients with subarachnoid hemorrhage, and two aneurysms were truly incidental.

Twenty-seven aneurysms were located in the anterior circulation(carotid cave 5, ventral paraclinoid 1, superior hypophyseal 1, posterior communicating 6, anterior choroidal 2, ICA bifurcation 2, anterior communicating 6, A2 4) and eight in the posterior circulation(PICA 2, AICA 1, SCA 2, BB 3). The demographic presentation and result are summarized in Table 1.

The procedures were performed under local anesthesia maintaining deep sedation by Propofol(Diprivan®, AstraZeneca, Caponago, Italy) continuous intravenous infusion and lidocaine infiltration at the femoral puncture site. Heparinized saline was flushed continuously through the catheters during procedure. A bolus of Heparin from 1000 to 2000 IU was given after the first coil deployed and at the end of the procedure. When the Neuroform stent(Boston Scientific, Fremont, CA) was deployed, oral antiplatelet agents(Aspirin 100mg and Plavix 75mg) were given postoperatively during various period from

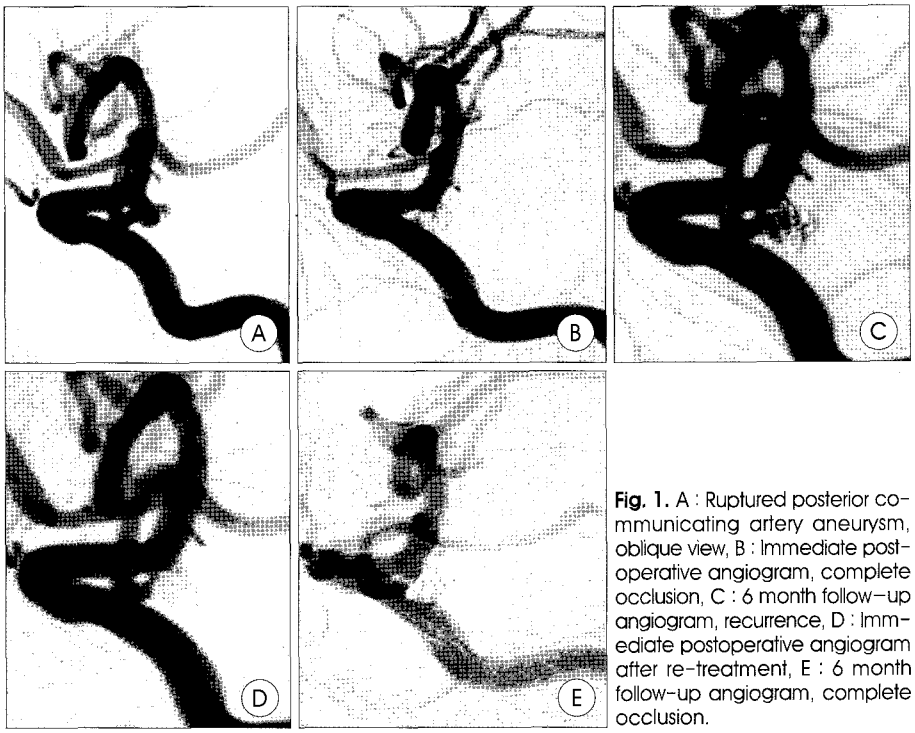

Fig. 1. A : Ruptured posterior communicating artery aneurysm, oblique view, B : Immediate postoperative angiogram, complete occlusion, C : 6 month follow-up angiogram, recurrence, D : Immediate postoperative angiogram after re-treatment, E : 6 month follow-up angiogram, complete occlusion.

two to four weeks. Any antiplatelet agents did not given preoperatively to the patients expecting use of Neuroform stent. The aneurysms were embolized by packing as densely as possible with Matrix coils. Embolization was stopped when the last coil could not be introduced into the sac, when angiographically complete obliteration was achieved, or when there was a danger of occluding the normal vascular branch next to the aneurysm or parent artery.

For statistical analysis, the size of each aneurysm was measured in three planes(length, width, and height) on anteroposterior and lateral digital subtraction angiography. To calculate the volume of the aneurysmal sac(Va) before embolization, we used the formula

$Va(mm^3)$ = length × width × height × 0.5.

We used this formula rather than the formula $V = 3 \times \pi \times$ length × width × height / 4, because the shape of the aneurysm was very irregular. We calculated coil volumes(Vc) with the formula $Vc=\pi (R/2)^2 \times L \times 10$, where L is the coil length in centimeters and R is the coil diameter. The diameters of Matrix coil are published by Boston Scientific and unit of inches converted into millimeters by computer. The packing ratio(%) of the aneurysm was obtained from the formula % = 100 (Vc / Va, and angiographic result was classified as complete, dog-ear, residual neck, and residual sac. Follow-up angiography was obtained in 16 patients after 6 months from the procedure. The oneway ANOVA test was used for statistical analysis, and differences of $P<0.05$ were considered statistically significant.

Results

The mean volume of the aneurysms was $83.6 \pm 99.8 mm^3$ ranging from $7.5 mm^3$ to $427.5 mm^3$. Mean packing ratio was $30.2 \pm 14.5\%$ ranging from 7.8% to 64.0%. On immediate angiography, complete occlusion of the aneurysm was achieved in 17 patients(48.6%), contrast filling around the neck in 8 patients(22.8%), and residual sac in 10 patients(28.6%). The Neuroform stent was used in 7 aneurysms to protect parent artery from coil herniation. In Neuroform group, complete occlusion was achieved in 2 of 7 aneurysms(28.6%). Non-Neuroform group achieved complete occlusion in 14 of 28 aneurysms(50.0%). Thromboembolism near the aneurysm neck occurred in two aneurysms and managed postoperatively by continuous intravenous injection of heparin. These patients had no clinical symptoms. Coil herniation and subsequent occlusion of parent artery occurred in two aneurysms located in A2 segment of the anterior cerebral artery and anterior communicating artery. The A2 aneurysm was managed by continuous intravenous injection of heparin postoperatively and recovered without any neurological deficit. Anterior communicating artery aneurysm resulted narrowing of anterior cerebral artery and distal thromboembolism. The herniated coil was removed and intra-arterial abcximab injection through microcatheter was followed. Finally, the artery was re-opened maintaining the aneurysm occluded completely, but fatal hemorrhage occurred two hours after the procedure.

Factors affecting angiographic results

We analyzed the relationship between aneurysm geometry and angiographic results. Volume of the aneurysm and coil packing ratio, dome-to-neck ratio measured along and across the parent artery, dome-to-height ratio, neck diameter measured along and across the parent artery, and use of Neuroform stent were regarded as factors affecting angiographic result, but there were no statistical significances between these factors and angiographic results(Table 2).

Follow-up results

There was no delayed bleeding or rebleeding during the follow-up period. Sixteen patients had angiographic follow-

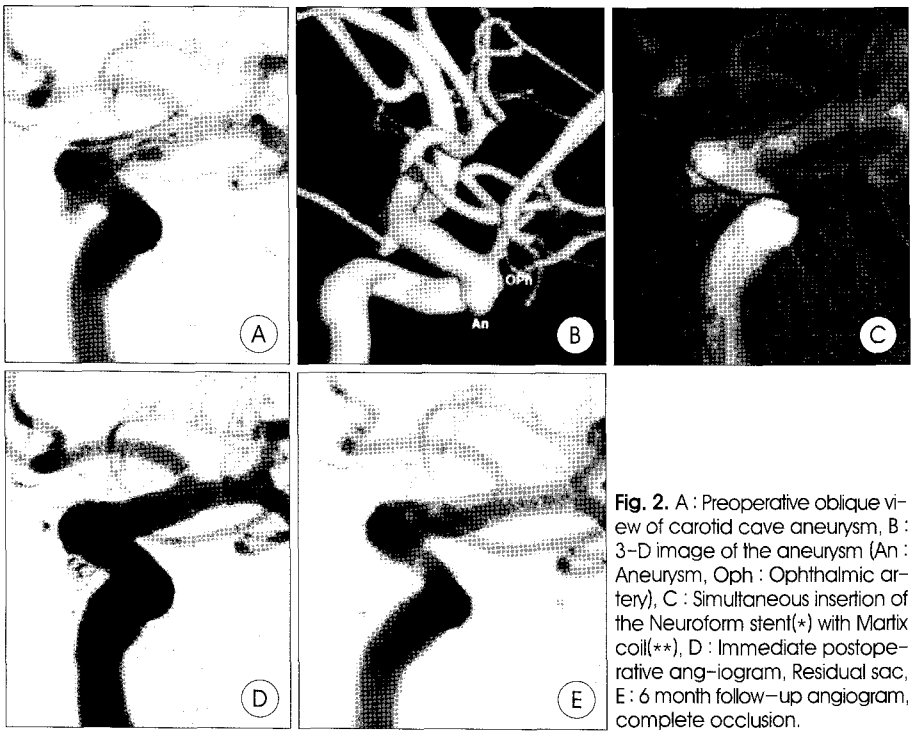

Fig. 2. A : Preoperative oblique view of carotid cave aneurysm, B : 3-D image of the aneurysm (An : Aneurysm, Oph : Ophthalmic artery), C : Simultaneous insertion of the Neuroform stent(*) with Martix coil(**), D : Immediate postoperative ang-iogram, Residual sac, E : 6 month follow-up angiogram, complete occlusion.

up after 6 months from the procedure. Fourteen patients showed complete occlusion(77.8%). Among 17 patients who showed complete occlusion on immediate postoperative angiography, 8 patients had follow-up angiography and one of them showed coil compaction and required re-treatment (Fig. 1). The others maintained complete occlusion. Two of eight patients who showed filling around the neck had follow-up angiography, and one remained residual neck and the other converted into complete occlusion. Five of ten patients followed in the group of residual sac, and all of them showed complete occlusion on follow-up angiography. Four of them were needed Neuroform stents to deploy the coils in the aneurysm safely.

In summary, on follow-up angiography of 16 aneurysms, 9 aneurysms remained unchanged (50%, complete 1, residual neck 1), 6 aneurysms more improved than immediate result (from residual neck to complete 1, from residual sac to complete 5, improving rate 37.5%). Only one aneurysm aggravated from complete to residual neck due to coil compaction (Compaction rate 6.3%, Fig. 1).

The characteristics of the improved 6 aneurysms are quite different from them of overall aneurysm. The mean volume of these aneurysms is 35.8mm^3, mean packing ratio is 19.2% ranging from 7.5% to 30.7%, dome-to neck ratio in length is 1.1 and 1.2 in width, and dome-to height ratio is 1.0. Four of these aneurysms treated with Neuroform stent because of their poor geometry. Because this stent, unlikely other coronary stents, has minimal effect in blocking the inflow of the blood stream and reactive endothelial hypertrophy, we regarded these improving result is due to the co-polymer action or characteristics of small sized aneurysm (Fig. 2). In our study, smaller aneu-rysms had a tendency to achieve complete occlusion difficultly with Matrix coil, but a tendency to ac-hieve higher rate of improvement on follow-up angiography.

Discussion

Long-term durability of the coiled aneurysm is one of the main concerns of endovascular treatment of the cerebral aneurysms. Coils are expected to disrupt blood flow entering aneurysm sac immediately after embolization, and to facilitate intra-aneurysmal thrombosis, organization and fibrosis. Ultimately, endothelial regenera-tion should occur to completely separate the aneurysm and to prevent recurrence. A platinum coil elicits a mild biological response when deployed into the aneurysm. Histopathologic studies of human aneurysms embolized with GDC reported slow organization of intra-aneurysmal clot[2,3,9,11,14-16,20,22,25]. Therefore, several investigators evaluated a modified platinum coil using bioactive materials to accelerate the biological mechanism that induces clot organization and fibrosis[1,4,6,8,13,18,21,23,24].

Matrix detachable coil is a newly designed hybrid platinum/BPM(bioabsorbable polymeric material) coil covered with a polyglycolic-polylactic acid(PGLA) copolymer. PGLA produces mild inflammatory reaction in the intra-aneurysmal clot constantly and degrades slowly over three months resulting more clot maturation than GDC. In swine aneurysm model, Murayama et al reported thicker neointimal and neoendothelial coverage of the neck of aneurysms and progressive aneurysm size reduction compared to GDC[17,19]. On the other hand, Ding et al reported that the Matrix group showed an increase in inflammation and coil compaction compared with HydroCoils(MicroVention, Aliso Viejo, CA) and platinum coils in experimental aneurysms of rabbits[11]. Linfante, et al reported follow-up results of 11 human aneurysms treated with Matrix only[6]. There was no recanalization at 12-month, but significant aneurysmal size reduction was not observed. Our study demonstrated that the Matrix coil is effective in preventing rupture or re-rupture and in improving angiographic results of incompletely occluded aneurysms.

It was well known that geometry of the aneurysm affects coil packing and angiographic result. The factors affecting aneurysm occlusion are dome-to neck ratio, dome-to-height ratio, aneurysm size, and absolute neck diameter, etc[5,9,26]. But these factors are now being relatively well dealt with than the past by various technique and materials. Double catheter technique and various neck remodeling techniques are widely shared and an open cell type self expanding nitinol stents were developed to cover the broad neck aneurysm. Therefore, indications for aneurysm coiling has been expanded than past. This situation, of necessity, focuses our attention to durability of the coiled aneurysm.

Clot maturation and neoendothelial coverage require precondition that the coil packed enough in the aneurysm and around the neck and this coil mesh tolerate hemodynamic stress during clot organization. In this point, Matrix coil system has several disadvantages. First, co-polymeric coating makes the coil less flexible and makes surface rough, so compact coil packing is difficult than bare platinum coil. Second, the core platinum coil of the Matrix is thinner than the GDC resulting in structural weakness, especially when clot maturation ended incompletely. These shortages are improving by newer version of Matrix coil system.

In our follow-up angiography, recurrence or aggravation of the aneurysm occurred in 1 of 16 aneurysms(6.3%). On the other hand, angiographic improvement from incomplete occlusion to complete occlusion achieved in 6 of 7 aneurysms(85.7%).

Conclusion

In spite of difficulty in achieving complete occlusion of Matrix coil system, there was no rupture or re-rupture during follow-up period. Follow-up angiography showed many conversion of residual sac into complete occlusion. Embolization using Matrix coil system is safe and effective, but the effects of PGLA copolymer need further investigation.

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Commentary

In this very interesting article, authors reviewed their short-term experience of the endovascular aneurysm treatment with PGLA(polyglycolic-polylactic acid)-coated coils(Matrix® coil, Boston Scientific, Fremont, CA). As they described, initial complete occlusion rate is about 48.6% and incomplete occlusion rate is 51.4%. In the follow-up angiogram, six of seven incompletely embolized aneurysms converted to complete occlusion and one of nine completely occluded aneurysms showed coil compaction. These results seem to be very encouraging considering relatively higher compaction rate in the follow-up studies when using uncoated coils for embolization. But, there are several discussing points in their results. First, follow-up terms are too short, only six month follow-up. As we can expect coil compaction could occur even after six months, more long-term follow-up study is mandatory for confirmation of stability. Second, in assessing the follow-up angiographic results, we should keep in mind that the initial location of aneurysm is very important factor in recurrence. As we know, basilar top aneurysm and posterior communicating artery aneurysm are prone to coil compaction. But, in this article, only two of six posterior communicating artery aneurysms and one of three basilar top aneurysms have follow-up angiograms and all of five small carotid cave aneurysms have follow-up angiograms. Third, they did not take into consideration of using the Neuroform® stent(Boston Scientific, Fremont, CA) in assessing the angiographic results. In my opinion, stent may have some role in the follow-up angiographic results. If we use Neuroform® stent to treat small aneurysm, initial complete packing is difficult, but these cases tend to convert to complete occlusion in the follow-up angiogram. I really want to congratulate the authors for their good results and expect their long-term follow-up results of these promising materials for cerebral aneurysms.

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