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Risk Factors for Recurrence after Endovascular Treatment of Saccular Cerebral Aneurysms

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Abstract

Background and Purpose: Endovascular coiling is the established standard treatment for managing both unruptured and ruptured cerebral aneurysms worldwide, but long-term durability remains inferior to surgical clipping. We investigated the risk factors for recurrence after endovascular treatment of cerebral aneurysms.

Materials and Methods: Between April 2012 and Aug 2016, we treated 92 patients with 95 saccular cerebral aneurysms. Aneurysms were categorized as side-wall or bifurcation type based on their morphology.

Results: We included 72 patients; 31 aneurysms were classified as side-wall aneurysms, and two had an axis parallel to the parent artery. Forty-one bifurcation aneurysms had an axis either perpendicular (n=23) or parallel (n=18) to the parent artery. Twelve recurrences (16.7%) were observed during follow-up, and nine underwent retreatment after 3–25 months. All retreatments were performed endovascularly without subsequent neurological complications. In univariate analysis, aneurysm dome size, neck width, cerebral aneurysms with an axis parallel to the parent artery, and incomplete occlusion showed statistically significant associations with recurrence. In multivariate Cox regression analysis, dome size (hazard ratio: 1.38; 95% CI: 1.06–1.97; p=0.013); branch incorporation (hazard ratio: 5.76; 95% CI: 1.05–35.66; p=0.042); and axis parallel to the parent artery (hazard ratio: 33.04; 95% CI: 4.47–430.36; p=0.0004) remained risk factors for recurrence.

Conclusion: Dome size, cerebral aneurysms with an axis parallel to the parent artery, and branch incorporation were significant factors for recurrence after endovascular coiling. More meticulous embolization and follow-up or alternative methods of changing blood flow into the aneurysm are necessary in this subgroup of patients.

Abbreviations

CI = Confidence Interval

Introduction

Since the publication of the International Subarachnoid Aneurysm Trial [1], endovascular coiling has been the accepted standard treatment to manage both ruptured and unruptured cerebral aneurysms. Advancements in endovascular technology and techniques have increased the safety of endovascular treatment for the majority of cerebral aneurysms [2,3]. However, the major drawback of endovascular treatment compared with surgical clipping is that long-term durability is inferior especially for large aneurysms [4-6]. A meta-analysis by Ferns et al. [6] showed that aneurysms recurred in 20.8% of patients, and retreatment was performed in 10.3%. In contrast, the reported recurrence rate after surgical clipping was less than 5% [7]. Both coil compaction and aneurysm sac growth are considered the principal mechanisms of recanalization after coil embolization [8]. We prospectively collected data for all patients treated by endovascular treatment between 2012 and 2016, at Kyoto Medical Center. We investigated the incidence of recurrence in clinical practice and identified the risk factors significantly associated with angiographic recurrence after endovascular treatment of cerebral aneurysms.

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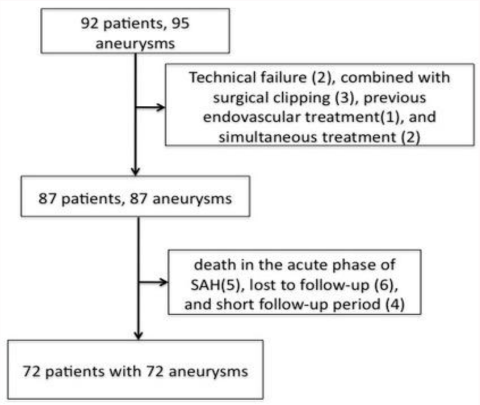

Figure 1: Flowchart shows the selection protocol for patients with cerebral aneurysms treated by endovascular coiling.

Methods

Patients

Ninety-two patients with 95 saccular cerebral aneurysms were endovascularly treated at the National Hospital Organization Kyoto Medical Center between April 2012 and Nov 2016. We retrospectively included patients who were followed-up for at least six months with available follow-up head magnetic resonance angiography or cerebral angiography results. We excluded patients with dissecting or blood blister-like aneurysms, those who were treated with both coiling and surgical clipping and patients who underwent endovascular retreatment. After exclusions, 72 patients met the study criteria and constituted our study population. Eight patients had multiple aneurysms, and three of these patients had two aneurysms treated endovascularly. In two multiple aneurysm patients, because two aneurysms were in the same location and treated simultaneously, only one aneurysm was included in the analysis. In one patient with ruptured anterior communicating aneurysm and an unruptured basilar artery aneurysm, only the basilar artery aneurysm was included in the analysis because the anterior communicating aneurysm was bilobed and treated with coiling combined with surgical clipping. We excluded patients from the study because of treatment failure (n=2), death in the acute phase of subarachnoid hemorrhage (n=5), treatment with coiling combined with surgical clipping (n=2), patient lost to follow-up (n=6), and short follow-up period (n=5) (Figure 1). Aneurysms were categorized as side-wall or bifurcation type, based on their location. Thirty-one aneurysms were classified as side-wall aneurysms, and two of these had an axis parallel to the parent artery, as described previously [9]. Forty-one bifurcation aneurysms had an axis either perpendicular (n=23) or parallel (n=18) to the parent artery.

Endovascular treatment

The median size of treated aneurysms was 5 mm (range, 2–23 mm). Dual antiplatelet premedication (100 mg acetylsalicylic acid plus 75 mg clopidogrel or 200 mg cilostazol) was administered to all patients with unruptured aneurysms. Antiplatelet premedication (40 mg ozagrel sodium and 200 mg cilostazol with or without 200 mg acetylsalicylic acid and 300 mg clopidogrel) was administered to three patients with ruptured aneurysms who were treated by stent-assisted coiling. Antiplatelet premedication (100–200 mg cilostazol with or without 200 mg acetylsalicylic acid or 40 mg ozagrel sodium) was given to eight other patients with ruptured aneurysms. Almost all of the patients with ruptured aneurysms were treated under general anesthesia, whereas almost all of the patients with unruptured aneurysms were treated using local anesthesia. Anticoagulation was initiated by an intravenous injection of a bolus of 2000–5000 IU heparin just after introducer sheath placement to increase the activated clotting time by 2- to 2.5 times above baseline. In ruptured cases, the activated clotting time was gradually increased during the procedure. In 44/72 procedures, endovascular coiling was performed using the single-catheter technique with various types of coils. In the other procedures, balloon-remodeling (n=15), stent-assisted (n=8), and double-catheter (n=8) techniques were used based on the aneurysm geometry. In three procedures, the double-catheter technique was combined with stent-assisted or balloon-remodeling techniques. The immediate angiographic outcomes were classified into three categories, as previously published by Roy et al. [10]. All patients with major recurrences were retreated endovascularly.

Clinical and angiographic follow-up

Patients were clinically assessed by neurosurgeons before and after treatment, just prior to discharge, and during clinical follow-up. Functional outcomes were evaluated using the modified Rankin scale score. Follow-up magnetic resonance angiography was used to evaluate recurrence for most cases at 6, 12, and 24 months after the procedures. When recurrence was suspected based on follow-up magnetic resonance angiography, catheter angiography was also performed. Recurrence was defined as any increase in the size of the remnant, and follow-up angiographic results were classified into three categories: stable or improved occlusion, minor recurrence requiring no retreatment, or major recurrence requiring retreatment. The median follow-up period was 15 months (range, 6–44 months).

Statistical analysis

All statistics were evaluated (or performed) by a statistician (N. Y.).We described frequency and percentage for binary data. Distribution of continuous variables was described by means and standard deviation. Univariate Cox regression analysis was performed to assess the association between a possible risk factor and recurrence, and we performed multivariate Cox regression with four variables that are well-known risk factors for recurrence [4-6,10-12] based on Raymond-Roy classification (class 3 *vs.* 1, 2), dome size, neck width, location (internal carotid-posterior communicating vs. other), and the two variables, branch incorporation and cerebral aneurysm axis to the parent artery. Variable selection in the model was performed by backward selection [13]. All P-values are two-sided, and the level of statistical significance was defined as $p<0.05$. All statistical analyses were performed using JMP software for Mac, version 11 (SAS software, Cary, NC).

Results

Study population

Our study included 24 men and 48 women, with ages ranging from 20–86 years (median, 66 years). Thirty-one patients had unruptured aneurysms, and 41 patients presented with subarachnoid hemorrhage, including one who experienced subarachnoid hemorrhage several years earlier and was initially treated conservatively.

Procedure outcomes

Patients' demographic and clinical characteristics and the treatment results are summarized in Table 1. Aneurysms were located on the internal carotid artery in 34 (47%) patients, middle

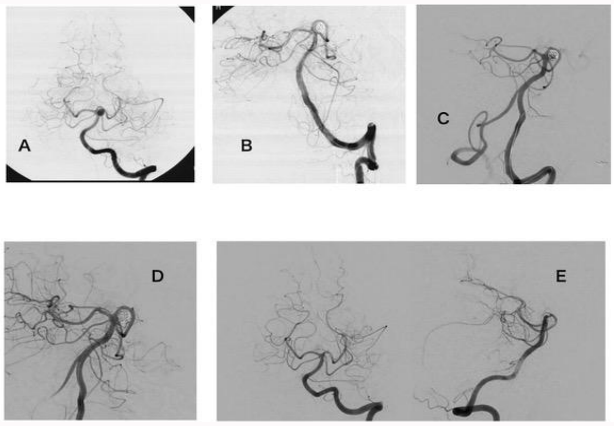

Figure 2: Images from a 63-year-old man with an unruptured aneurysm at the left basilar artery-superior cerebellar artery. A, anteroposterior view of a left vertebral angiogram shows a saccular aneurysm at the left basilar artery-superior cerebellar artery. B, Postprocedural angiogram shows adequate occlusion of the aneurysm while preserving the superior cerebellar artery using a balloon-remodeling technique. C, Follow-up angiogram at 12 months after treatment shows major recanalization of the aneurysm. D, Retreatment was performed using stent-assisted coil embolization. An Enterprise VRD 4.5 mm × 22 mm stent was deployed through the basilar artery to the left posterior cerebral artery, and the curved basilar artery was linearized. E, Biplanar image of the last follow-up angiograms at 25 months shows stable occlusion of the aneurysm and linearization of the basilar artery.

Table 1: Summary of demographic and clinical characteristics of 72 patients.

characteristics	number
Sex	
Male	24 (33.3%)
female	48 (66.7%)
Age	
<50	12 (16.7%)
50-59	14 (19.4%)
60-69	22 (30.6%)
70-79	17 (23.6%)
>=80	7 (9.7%)
Presentation	
Ruptured	41 (56.9%)
unruptured	31 (43.1%)
size	
<5mm	31 (43.1%)
5-10mm	36 (50%)
>=10mm	5 (6.9%)
location	
Internal carotid artery	34 (47.2%)
Anterior cerebral artery	19 (26.4%)
Middle cerebral artery	8 (11.1%)
Vertebrobasilar system	11 (15.3%)
Branch incorporation	
Dome	1 (1.4%)
Neck	25 (34.7%)
None	46 (63.9%)
neck	
<4mm	51 (70.8%)
>=4mm	21 (29.2%)
Shape	
Round	38 (52.8%)
Irregular	34 (47.2%)
Axis to the parent artery	
Parallel	20 (27.8%)
Perpendicular	52 (72.2%)
Adjunctive technique	
Simple technique	44 (61.1%)
Balloon remodeling technique	15 (20.8%)
Stent-assisted embolization	8 (11.1%)
Double catheter technique	8 (11.1%)
Raymond Roy classification	
Class 1	31 (43.1%)
Class 2	32 (44.4%)
Class 3	9 (12.5%)
Functional outcome	
mRS 0	45 (62.5%)
mRS1, 2	19 (26.4%)
mRS3-5	8 (11.1%)

cerebral artery in 8 (11%), anterior cerebral artery in 19 (26%), and vertebrobasilar system in 11 (15%). Postembolization angiography revealed complete occlusion in 31 (43%) aneurysms, neck remnant in 32 (44%), and incomplete occlusion in 8 (13%). No patients with unruptured aneurysms had a change in modified Rankin scale score after treatment. Thirty-four of 41 (83%) patients with ruptured aneurysms had favorable outcomes. Overall, 64 patients (89%) had favorable outcomes (modified Rankin scale, 0–2) at 90 days after treatment. However, one patient died after 6 months because of multiple organ failure secondary to sepsis unrelated to the procedure or the cerebral aneurysm.

Recurrences

Recurrences occurred in 12 (15.7%) of the treated aneurysms, as shown in Table 2. Recurrent aneurysms were located on the internal carotid-posterior communicating artery in seven cases, middle cerebral artery in one, anterior communicating artery in two, and basilar artery in two. Nine recurrent patients were retreated

Table 2: Summary of recurrent cases.

age, sex	location,	presentation	size (mm)	type, axis	1st procedure	1st outcome	interval (months)	2nd procedure	2nd outcome	mRS
39, female	IC-Pcom,	ruptured	8	side wall, perpendicular	balloon-remodeling	neck remnant	13	stent-assisted	nearly complete occlusion	0
57, female	IC-Pcom	ruptured	5	side wall, perpendicular	single catheter	neck remnant	22	stent-assisted	nearly complete occlusion	0
66, female	IC-Pcom,	ruptured	5	side wall, perpendicular	single catheter	neck remnant	22	stent-assisted	nearly complete occlusion	0
80, female	IC-Pcom	unruptured	10	side wall, perpendicular	stent-assisted	incomplete	14	single catheter	incomplete	1
85, female	IC-Pcom	unruptured	5	side wall, perpendicular	stent-assisted	neck remnant	9	-	-	0
71, female	IC-Pcom	ruptured	22	side wall, parallel	single catheter	incomplete	3	balloon-remodeling	neck remnant	5
71, male	Acom	unruptured	8	bifurcation, parallel	single catheter	neck remnant	12	-	-	3
36, female	MCA	ruptured	4	side wall, perpendicular	single catheter	nearly complete	5	single catheter	nearly complete occlusion	0
63, male	BA-SCA	unruptured	5	bifurcation, parallel	single catheter	nearly complete	13	stent-assisted	complete occlusion	0
59, female	BA top	unruptured	12	bifurcation, parallel	stent-assisted+double catheter	neck remnant	25	double catheter	neck remnant	0
80, female	IC-Pcom	ruptured	7	side wall, parallel	balloon-remodeling	incomplete	8	stent-assisted	incomplete	3
62, male	Acom	Unruptured	7	Bifurcation, parallel	Simple	Incomplete	12	-		0

Table 3: Association between potential risk factors and recanalization after coil embolization of cerebral aneurysms were assessed using univariate Cox regression analysis.

factor	recurrence	risk ratio (95% confidence interval)	p value
sex		0.91 (0.20-3.10)	0.891
female(48)	9 (18.7%)		
male(24)	3 (12.5%)		
presentation		1.33(0.41-4.27)	0.622
ruptured(41)	6 (14.6%)		
unruptured(31)	6 (19.4%)		
number of aneurysm		2.38(0.53-7.97)	0.231
single(64)	9(13.9%)		
multiple(8)	3(37.5%)		
shape		2.96(0.93-11.15)	0.067
round(38)	4 (10.5%)		
irregular(34)	8 (23.5%)		
axis to the parent artery		3.73(1.16-12.04)	0.029
perpendicular(52)	6 (11.5%)		
parallel(20)	6 (30.0%)		
location		2.92 (0.93-9.89)	0.066
other(50)	5 (10.0%)		
ICA-Pcom(22)	7 (31.8%)		
branch incorporation		2.95(0.93-9.97)	0.064
no(46)	5 (10.8%)		
yes(26)	7 (26.9%)		
stent assisted embolization		2.86(0.63-9.60)	0.153
without stent (64)	9 (14.1%)		
stent assisted embolization (8)	3 (37.5%)		
Raymond Roy classification		5.56(1.47-17.96)	0.014
1,2 (63)	8 (12.7%)		
3(9)	4 (44,4%)		
age		1.00(0.96-1.06)	0.887
Dome size		1.47(1.21-1.87)	<0.0001
Neck witdh		2.09(1.30-3.29)	0.035

endovascularly with no neurological sequelae. The timing of retreatment ranged from 3–25 months after the first procedure. In 5/9 repeat procedures, embolization was performed using a stent-assisted technique as shown in Figure 2. One of these patients experienced a second and third recurrence after retreatment with coils because of enlargement of the aneurysmal wall, and was eventually treated using a stent-assisted technique at 19 months. In one patient with a major recurrence, retreatment was suspended because of the patient's advanced age and concomitant chronic kidney disease. No patient experienced a bleeding episode during follow-up.

Factors associated with recurrences

The associations between potential clinical risk factors and recurrence after embolization are summarized in Table 2. In the Cox regression analysis, the variables aneurysm dome size (hazard ratio: 1.47; 95% confidence interval: 1.21–1.87; p<0.0001), neck width (hazard ratio: 2.09; 95% confidence interval: 1.30–3.29; p=0.035), cerebral aneurysm with an axis parallel to the parent artery (hazard ratio: 3.73; 95% confidence interval: 1.16–12.04; p=0.029), and incomplete occlusion (hazard ratio: 5.56; 95% confidence interval: 1.47–17.96; p=0.035) showed statistical significance (Table 3). Multivariate analysis revealed that cerebral aneurysm with an axis parallel to the parent artery (hazard ratio: 33.04; 95% confidence interval: 4.47–430.36; p=0.0004), dome size (hazard ratio: 1.38; 95% confidence interval: 1.06–1.97; p=0.013), and branch incorporation (hazard ratio: 5.76; 95% confidence interval: 1.05–35.66; p=0.042) remained statistically significant risk factors (Table 4).

Discussion

Endovascular coiling is the established standard treatment in managing both unruptured and ruptured cerebral aneurysms worldwide. However, most authors agree that the durability of endovascular treatment is inferior to that of surgical clipping [7,14]. The reported incidence of recanalization in a large prospective study was 5.5% to 33% [7,14-17]. Large aneurysmal size, posterior circulation

Table 4: Results of multivariate Cox regression analysis.

factors	harzard ration (95% CI)	p value
Raymond Roy classification (class 3 vs1,2)	1.01(0.15-6.38)	0.987
axis to the parent artery (parallel vs. perpendicular)	33.04(4.47-430.36)	0.0004
size	1.38 (1.06-1.97)	0.013
neck	1.21(0.43-3.32)	0.716
branch incorporation	5.76(1.05-35.66)	0.042
Location	5.00 (0.90-53.91)	0.067

aneurysms, wide neck, incomplete occlusion, low packing density, and ruptured aneurysms are reported risk factors for recurrence [4,6,12,18-20]. Although some clinical studies have included advanced technologies to gain more stability or packing density, including stent-assisted embolization [21,22], hydrogel-coated coils [23], and large-diameter coils [24], less durability remains the major drawback of endovascular coiling. In our series, the recanalization rate after coil embolization of ruptured and unruptured aneurysms was 16%, which was compatible with previous reports. In our univariate analysis, larger size, wider neck, and incomplete occlusion were associated with recanalization, as in previous studies.

Branch incorporation

Because of remarkable advances in endovascular techniques and technology, aneurysms with a branch incorporated into the aneurysmal wall can now be embolized without occluding the incorporated branch [25], which was considered difficult in the past. However, although it is now easier to preserve an incorporated branch, it remains difficult to balance the patency of the incorporated branch and treatment durability to prevent bleeding. Also, few data are available regarding long-term durability of endovascular coiling in this subgroup of cerebral aneurysms. To our knowledge, branch incorporation has not been investigated previously as a factor in recanalization after endovascular coiling.

Axis to the parent artery

It is well known that cerebral aneurysms at the tip of the basilar artery are likely to recur after embolization [26,27]. Basilar tip aneurysms are classified as bifurcation aneurysms and usually have an axis parallel to the parent artery. In our series, an axis parallel to the parent artery was the most significant predictor of recanalization, possibly because of a jet-pattern inflow for these aneurysms. Szikora et al. [9] reported that aneurysms with a main axis parallel to the parent artery have a tendency to have a jet-flow pattern and uneven distribution of unsteady pressure. We are currently conducting a clinical study to clarify the association between disturbed flow in the aneurysm and recurrence after embolization using computational flow-dynamic techniques [28]. We hypothesize that high-magnitude wall-shear stress and strong disturbed flow may be involved in aneurysm recurrence. However, our findings and hypothesis require confirmation in larger future studies.

Size

In our series, univariate analysis showed that aneurysm size was highly associated with recurrence, similar to previous studies [6,26]. Recurrence was observed in 3/6 (50%) aneurysms larger than 10 mm, which was compatible with previous studies reporting an incidence of recanalization after embolization of large or giant aneurysms as high as 39% [29]. Therefore, although a flow-diverting stent can be a promising option [30,31], further study is needed to establish the best method to treat large and giant aneurysms.

Limitations

There are certain limitations in our study. First, because of the retrospective nature, selection bias may be present. However, this bias may have been minimized by prospectively recording the data for aneurysms treated endovascularly into a database. A second limitation is the limited number of cases; our findings should be confirmed in a larger prospective study. A third limitation is that the follow-up period was relatively short; the median follow-up period was 15 months. However, all of the patients in this series had follow-up magnetic resonance imaging at 6–12 months, and all recurrences were observed within 12 months. Reopening of cerebral aneurysms is rare when adequate occlusion is confirmed at 6 months after embolization [32]. We found that the risks of recurrence associated with axis to the parent artery and branch incorporation were significant, but a slight data bias may be present [33] because these aneurysms had large hazard ratios and/or very wide confidence intervals on multivariable Cox regression.

Conclusion

In our cohort, the recanalization rate after coil embolization of ruptured and unruptured aneurysms was 16%. In addition to dome size, cerebral aneurysms with an axis parallel to the parent artery and branch incorporation were significant predictors of recurrence after endovascular coiling. More meticulous embolization and follow-up or alternative methods of changing flow into the aneurysm are necessary in this subgroup of patients.

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References

1. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet. 2002;360:1267-74.
2. Brinjikji W, Rabinstein AA, Lanzino G, Kallmes DF, Cloft HJ. Patient outcomes are better for unruptured cerebral aneurysms treated at centers that preferentially treat with endovascular coiling: a study of the national inpatient sample 2001-2007. AJNR Am J Neuroradiol. 2011;32:1065-70.
3. Brinjikji W, Rabinstein AA, Nasr DM, Lanzino G, Kallmes DF, Cloft HJ. Better outcomes with treatment by coiling relative to clipping of unruptured intracranial aneurysms in the United States, 2001-2008. AJNR Am J Neuroradiol. 2011;32:1071-75.
4. Campi A, Ramzi N, Molyneux AJ, Summers PE, Kerr RS, Sneade M, et al. Retreatment of ruptured cerebral aneurysms in patients randomized by coiling or clipping in the International Subarachnoid Aneurysm Trial (ISAT). Stroke. 2007;38:1538-44.
5. van Rooij WJ, Sprengers ME, Sluzewski M, Beute GN. Intracranial aneurysms that repeatedly reopen over time after coiling: imaging characteristics and treatment outcome. Neuroradiology. 2007;49:343-9.
6. Ferns SP, Sprengers ME, van Rooij WJ, Rinkel GJ, van Rijn JC, Bipat S, et al. Coiling of intracranial aneurysms: a systematic review on initial occlusion and reopening and retreatment rates. Stroke. 2009;40:523-9.
7. Spetzler RF, McDougall CG, Zabramski JM, Albuquerque FC, Hills NK. The Barrow Ruptured Aneurysm Trial: 6-year results. J Neurosurg. 2015;123(3):609-17.
8. Hasan DM, Nadareyshvili AI, Hoppe AL, Mahaney KB, Kung DK,

Raghavan ML. Cerebral aneurysm sac growth as the etiology of recurrence after successful coil embolization. Stroke. 2012;43:866-8.

9. Szikora I, Paal G, Ugron A, Nasztanovics F, Marosfoi M, Berentei Z, et al. Impact of aneurysmal geometry on intraaneurysmal flow: a computerized flow simulation study. Neuroradiology. 2008;50(5):411-21.

10. Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. Stroke. 2001;32(9):1998-2004.

11. Wehman JC, Hanel RA, Levy EI, Hopkins LN. Giant cerebral aneurysms: endovascular challenges. Neurosurgery. 2006;59:S125-38.

12. Pierot L, Cognard C, Anxionnat R, Ricolfi F, Clarity Investigators. Endovascular treatment of ruptured intracranial aneurysms: factors affecting midterm quality anatomic results: analysis in a prospective, multicenter series of patients (CLARITY). AJNR Am J Neuroradiol. 2012;33:1475-80.

13. Robins JM, Greenland S. The role of model selection in causal inference from nonexperimental data. Am J Epidemiol. 1986;123(3):392-402.

14. Molyneux AJ, Birks J, Clarke A, Sneade M, Kerr RS. The durability of endovascular coiling versus neurosurgical clipping of ruptured cerebral aneurysms: 18 year follow-up of the UK cohort of the International Subarachnoid Aneurysm Trial (ISAT). Lancet. 2015;385:691-7.

15. White PM, Lewis SC, Gholkar A, Sellar RJ, Nahser H, Cognard C, et al. Hydrogel-coated coils versus bare platinum coils for the endovascular treatment of intracranial aneurysms (HELPS): a randomised controlled trial. Lancet. 2011;377:1655-62.

16. Coley S, Sneade M, Clarke A, Mehta Z, Kallmes D, Cekirge S, et al. Cerecyte coil trial: procedural safety and clinical outcomes in patients with ruptured and unruptured intracranial aneurysms. AJNR Am J Neuroradiol. 2012;33:474-80.

17. McDougall CG, Johnston SC, Gholkar A, Barnwell SL, Vazquez Suarez JC, Masso Romero J, et al. Bioactive versus bare platinum coils in the treatment of intracranial aneurysms: the MAPS (Matrix and Platinum Science) trial. AJNR Am J Neuroradiol. 2014;35:935-42.

18. Raymond J, Guilbert F, Weill A, Georganos SA, Juravsky L, Lambert A, et al. Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. Stroke. 2003;34:1398-403.

19. Ogilvy CS, Chua MH, Fusco MR, Griessenauer CJ, Harrigan MR, Sonig A, et al. Validation of a System to Predict Recanalization After Endovascular Treatment of Intracranial Aneurysms. Neurosurgery, 2015;77:168-73.

20. 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;231:653-8.

21. Geyik S, Yavuz K, Yurttutan N, Saatci I, Cekirge HS. Stent-assisted coiling in endovascular treatment of 500 consecutive cerebral aneurysms with long-term follow-up. AJNR Am J Neuroradiol. 2013;34(11):2157-62.

22. Nishido H, Piotin M, Bartolini B, Pistocchi S, Redjem H, Blanc R. Analysis of complications and recurrences of aneurysm coiling with special emphasis on the stent-assisted technique. AJNR Am J Neuroradiol. 2014;35:339-44.

23. Brinjikji W, White PM, Nahser H, Wardlaw J, Sellar R, Cloft HJ, et al. HydroCoils reduce recurrence rates in recently ruptured medium-sized intracranial aneurysms: a subgroup analysis of the HELPS trial. AJNR Am J Neuroradiol. 2015;36:1136-41.

24. Milburn J, Pansara AL, Vidal G, Martinez RC. Initial experience using the Penumbra coil 400: comparison of aneurysm packing, cost effectiveness, and coil efficiency. J Neurointerv Surg. 2014;6(2):121-4.

25. Kim BM, Park SI, Kim DJ, Kim DI, Suh SH, Kwon TH, et al. Endovascular coil embolization of aneurysms with a branch incorporated into the sac. AJNR Am J Neuroradiol. 2010;31(1):145-51.

26. Ferns SP, Sprengers ME, van Rooij WJ, van Zwam WH, de Kort GA, Velthuis BK, et al. Late reopening of adequately coiled intracranial aneurysms: frequency and risk factors in 400 patients with 440 aneurysms. Stroke. 2011;42:1331-7.

27. van Eijck M, Bechan RS, Sluzewski M, Peluso JP, Roks G, van Rooij WJ. Clinical and Imaging Follow-Up of Patients with Coiled Basilar Tip Aneurysms Up to 20 Years. AJNR Am J Neuroradiol. 2015;36(11):2108-13.

28. Shimogonya Y, Fukuda S. Computational and experimental studies into the hemodynamics of cerebral aneurysms. J Biomechanical Science and Engineering. 2016;11;15-488.

29. Chalouhi N, Tjoumakaris S, Gonzalez LF, Dumont AS, Starke RM, Hasan D, et al. Coiling of large and giant aneurysms: complications and long-term results of 334 cases. AJNR Am J Neuroradiol. 2014;35(3):546-52.

30. Becske T, Kallmes DF, Saatci I, McDougall CG, Szikora I, Lanzino G, et al. Pipeline for uncoilable or failed aneurysms: results from a multicenter clinical trial. Radiology. 2013;267(3):858-68.

31. Szikora I, Berentei Z, Kulcsar Z, Marosfoi M, Vajda ZS, Lee W, et al. Treatment of intracranial aneurysms by functional reconstruction of the parent artery: the Budapest experience with the pipeline embolization device. AJNR Am J Neuroradiol. 2010;31:1139-47.

32. Sprengers ME, Schaafsma J, van Rooij WJ, Sluzewski M, Rinkel GJ, Velthuis BK, et al. Stability of intracranial aneurysms adequately occluded 6 months after coiling: a 3T MR angiography multicenter long-term follow-up study. AJNR Am J Neuroradiol. 2008;29:1768-74.

33. Greenland S, Mansournia MA, Altman DG. Sparse data bias: a problem hiding in plain sight. BMJ. 2016;352:i1981.