Online April 7, 2021
Journal of Neuroendovascular Therapy 2021; 15: 793–799 DOI: 10.5797/jnet.oa.2020-0212

Original Article

Follow-Up DSA at Day 9 ± 2 after Subarachnoid Hemorrhage Predicts Long-Term Recurrence of Ruptured Cerebral Aneurysm after Coiling

Norihito Shimamura,[1] Masato Naraoka,[2] Takeshi Katagai,[2] Nozomi Fujiwara,[2] Kosuke Katayama,[2] Takao Sasaki,[2] Shouhei Kinoshita,[2] Keita Yanagiya,[2] and Hiroki Ohkuma[2]

Objective: The recurrence rate of coiled ruptured cerebral aneurysms is greater than that of clipped aneurysms. The aim of this study is to determine the factors that relate to the recurrence of embolized, ruptured cerebral aneurysms, and the evidence thereto.

Methods: From April 2007 through July 2017, we treated 134 ruptured cerebral aneurysm cases by coiling. DSA and/or MRI were done in 98 saccular aneurysm cases one year after the coiling. Recurrence was defined as enlargement of the aneurysm neck or contrast opacification along the aneurysm wall. A chi-square test and a logistic regression analysis were done to analyze the relationship between aneurysm recurrence and clinical factors.

Results: The median follow-up period was 58 months (interquartile range [IQR]: 33–107). Ten cases (10.2%) were subjected to aneurysm recurrence. Internal carotid artery (ICA) aneurysms proximal to the posterior communicating artery, incomplete obliteration of an aneurysm at initial embolization and postoperative DSA during day 9 ± 2, and increased contrast medium in the aneurysm at postoperative DSA during day 9 ± 2 were all statistically related to the recurrence of the aneurysm. Logistic regression analysis showed that the increased contrast medium in the aneurysm at day 9 ± 2 was statistically related to aneurysm recurrence ($p < 0.0001$). Recurrence or retreatment of the aneurysm did not influence the outcome.

Conclusion: Complete obliteration of the aneurysm at the first session is important. Recurrence of an embolized ruptured aneurysm can be estimated by postoperative DSA at day 9 ± 2 days.

Keywords coiling, retreatment, ruptured cerebral aneurysm, subarachnoid hemorrhage

Introduction

Coil embolization of a ruptured cerebral aneurysm is a common procedure throughout the world. The risk of recurrence with re-bleeding is significantly higher than with clipping.[1,2] The rate of aneurysm recurrence is also related to the location of the aneurysm.[3–6] An internal carotid artery-posterior communicating artery (IC-PC) aneurysm and a basilar artery (BA) tip aneurysm showed a 9.3%–55% recurrence rate.[3,5,6] Advances in technology have continued to decrease the rate of recurrence of a coiled aneurysm from 8.8% to 4.8%.[5] However, the recurrence rate is not zero. Ten years after subarachnoid hemorrhage (SAH), the neurological status is similar for both clipping and coiling cases.[1,2] A reduction in recurrence and the prevention of re-rupture in a coiled aneurysm would thus be a great gift to SAH patients and their families.

We reviewed consecutive, coil embolized, ruptured cerebral aneurysms to help avoid associated pitfalls that include recurrence related to the location of the aneurysm and to achieve complete, long-term obliteration of a ruptured cerebral aneurysm. We analyzed the factors involved and the evidence thereto in relation to the recurrence of

[1]*Department of Neuroendovascular Therapy, Hirosaki University Graduate School of Medicine, Hirosaki, Aomori, Japan*
[2]*Department of Neurosurgery, Hirosaki University Graduate School of Medicine, Hirosaki, Aomori, Japan*

Received: December 25, 2020; Accepted: February 20, 2021
Corresponding author: Norihito Shimamura. Department of Neuroendovascular Therapy, Hirosaki University Graduate School of Medicine, 5, Zaihuchou, Hirosaki, Aomori 036-8562, Japan
Email: shimab@hirosaki-u.ac.jp

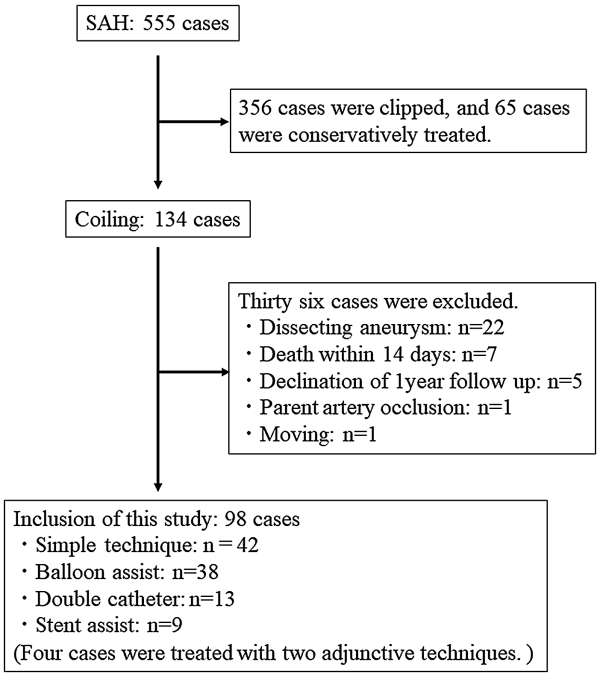

Fig. 1 Patient selection flowchart. SAH: subarachnoid hemorrhage

embolized ruptured cerebral aneurysms and we discuss the strategy for their complete embolization.

Materials and Methods

Patients

This study was approved by the Ethics Committee, with written, informed consent provided by patients and/or their families.

From April 2007 through July 2017, we treated 555 SAH cases. Selection of the treatment method was done based on the specific medical problems (e.g., lung edema, advanced age, posterior circulation, aneurysm size) by a certificated neurosurgeon and a certificated neuro-endovascular surgeon. Consecutively, 134 ruptured saccular cerebral aneurysm cases were treated by coil embolization (**Fig. 1**). In all, 36 cases were excluded from this study because of medico-social reasons. In total, 98 saccular aneurysm cases were included in this study, with MRI and/or DSA performed 1 year after the coiling (**Table 1**, supplemental table).

All patients were treated within 24 hours after admission to our department. Aneurysm neck clipping is the first-line therapy at our institute; coiling was done in 20% of aneurysms in all SAH cases during the analyzed period.

Treatment

Aneurysm coiling procedures were done by a certificated neuro-endovascular surgeon (NS). Tight coil packing was done to the extent possible in each case (**Figs. 2**, **3A**, and **3B**). Also, periprocedural antiplatelet therapy and anticoagulant therapy were done: A combination of 200 mg aspirin, 150 or 300 mg clopidogrel, and 200 mg cilostazol was administered more than 2 hours before coil embolization via a trans oral or a trans naso-gastric tube.[7] All adjunctive techniques were acceptable for this study (**Table 1**). Anticoagulant was administered after sheath insertion in all cases and continued 24 or 48 hours.

Table 1 Overview of analyzed cases

Content	Result
Age (median, IQR)	66.5 (54–77.5)
Gender (Male/Female)	23/75 (23%/77%)
Hunt-Kosnik grade (I–III: IV–V)	77/21 (79%/21%)
Aneurysm location (pIC: dIC: Acom: VBA: Others)	7: 33 :32: 21: 5 (7%: 34%: 33%: 21%: 5%)
Maximum aneurysm size (Mean ± SD)	8.1 mm ± 4.1
Aspect ratio (Mean ± SD)	2.0 ± 0.71
Adjunctive technique* (none: balloon: double catheter: stent)	42: 38: 13: 9 (43%: 39%: 13%: 9.2%)
Volume embolization ratio (Mean ± SD)	29% ± 10
Raymond–Roy classification at initial embolization (DF: NR: CO)	2: 25: 71 (2%: 26%: 72%)
Raymond–Roy classification at day 9 ± 2 days (DF: NR: CO)	3: 23: 72 (3%: 23%: 73%)
Glasgow Outcome Scale (GR and MD: SD, VS, and D)	76: 22 (78%: 23%)
Follow-up periods (Median, IQR)	58 months (33–107)
Recurrence of embolized aneurysm (%)	10 (10.2%)

*Four cases were treated with two adjunctive techniques. Acom: anterior communicating artery; CO: complete obliteration; D: death; DF: dome filling; dIC: distal internal carotid artery (C1); GR: good recovery; IQR: interquartile range; MD: moderately disabled; NR: neck remnant; pIC: proximal intradural carotid artery (C3~2); SD: severely disabled; VBA: vertebra-basilar artery; VS: vegetative state

Follow-up imaging

We selected formal post-coiling imaging analyses. Plain CT and/or MRI (DWI, FLAIR, and MRA) were done the day after coiling. DSA was done at day 9 ± 2 after the treatment for the purpose of diagnosing the obliteration of the aneurysm and cerebral vasospasm (**Figs. 2** and **3C**). MRI and MRA were taken 6 months after the ictus. DSA was done 1 year after the ictus (**Fig. 3E**). Several cases refused to allow DSA, an MRA was done for those cases. Yearly MR imaging was subsequently recommended.

Fig. 2 Definition of increased intra-aneurysmal blood flow. (**A**) Preoperative DSA. (**B**) Post-initial embolization. The arrow shows neck remnant. (**C**): Follow-up DSA at day 9. Blood flow into the aneurysm is increased (arrow), but the embolization status keeps neck remnant. The arrowheads represent vasospasm.

Definition of recurrence and indication of re-treatment

An aneurysm neck that appeared faint and for which physicians did not recommend additional treatment was not defined as recurrence (**Fig. 2**). Obvious enlargement of the residual aneurysm neck or contrast opacification along the aneurysm wall was defined as recurrence (**Fig. 3C**). Recurrence was judged by two blinded co-authors (KK and HO) and consensus meetings were held. We thereby recommended re-treatment of the aneurysm to the patient and their family (**Fig. 3D**). An aneurysm with contrast opacification along the aneurysm wall has an especially high risk of rupture,[8] and we recommend emergent or early retreatment.

Outcomes

We compared the recurrence group and the non-recurrence group regarding age, aneurysm location, aneurysm size, neck diameter, aspect ratio (height/neck width of aneurysm),[9] adjuvant treatment methods, volume embolization ratio (VER),[10] Raymond–Roy classification,[11] intraoperative complications, postoperative DSA during day 9 ± 2 after the ictus, and the Glasgow Outcome Scale at 1 year after the ictus.[12] Date collection was done by three blinded co-authors (TS, SK, and KY) and consensus meetings were held. Internal carotid artery (ICA) aneurysms were divided into proximal ICA and distal ICA at the branching of the posterior communicating artery.

Statistics

A Pearson's chi-square test or a Kruskal–Wallis analysis was used to analyze the relationship between aneurysm recurrence and clinical factors. Logistic regression analysis was done to detect factors related to aneurysm recurrence (JMP 12.0.1; SAS Institute, Cary, NC, USA). A p value below 0.05 was considered statistically significant.

Results

Median patient age was 66.5 years (interquartile range [IQR]: 54–77.5) and females accounted for 77% (**Table 1**). Maximum aneurysm size was 8.1 mm ± 4.1 SD and the aspect ratio was 2.0 ± 0.71 SD. Adjunctive techniques were selected in 57% of cases. At the end of initial coil embolization, 72% of aneurysms were occluded completely and the mean VER was 29% ± 10 SD. Long-term aneurysm imaging follow-up, with a median period of 58 months (IQR: 33–107), detected recurrence in 10 cases (10.2%), including one case of rebleeding.

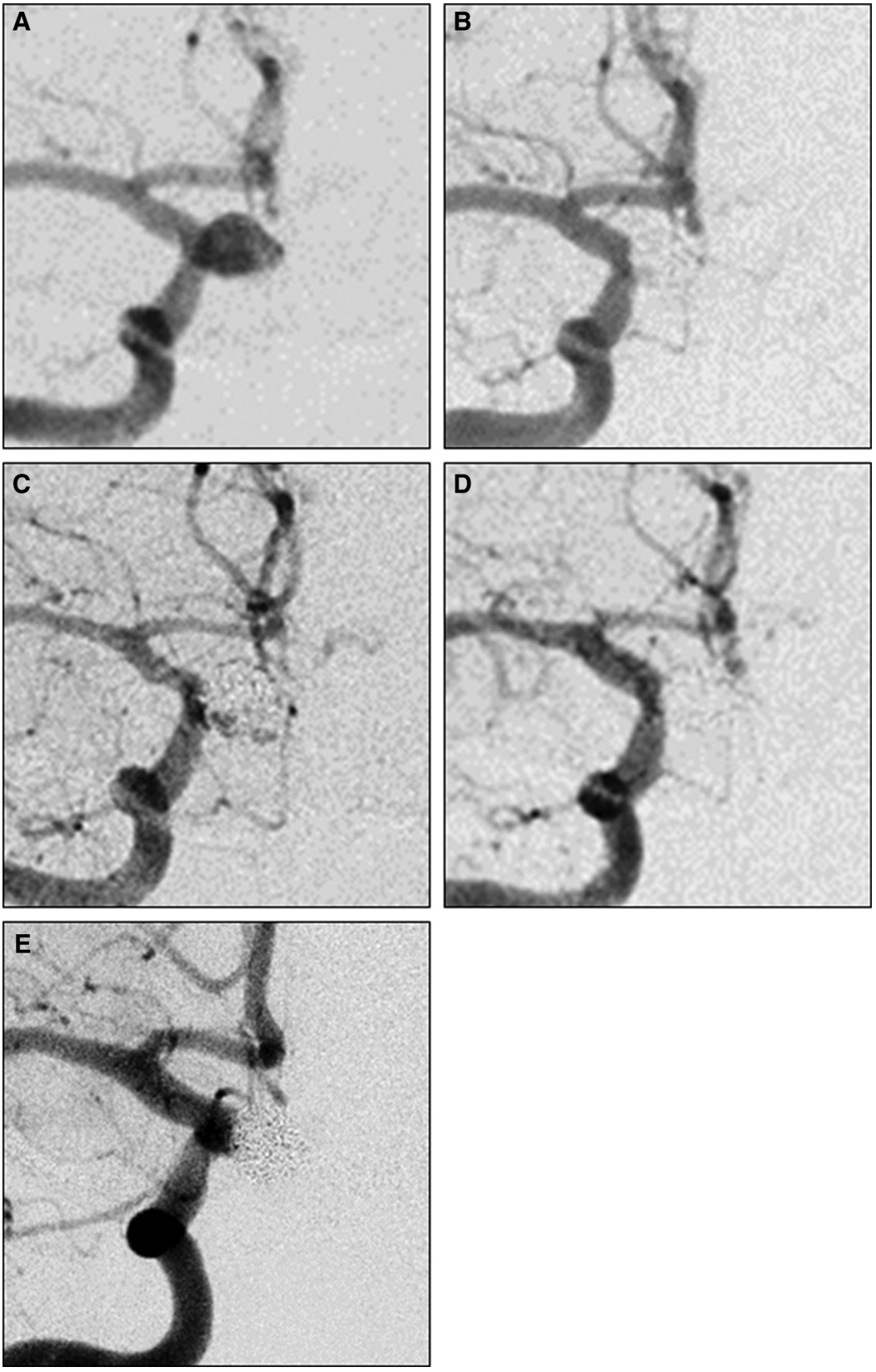

Fig. 3 DSA of retreatment of a ruptured right ICA paraclinoid aneurysm. (**A**) Preoperative DSA at day 0. (**B**) Post-initial embolization at day 0. Embolized status was neck remnant. (**C**) Follow-up DSA at day 7. Neck remnant of aneurysm worsened. (**D**) Post-re-embolization at day 24. Aneurysm was completely embolized. (**E**) One year after the re-embolization. Aneurysm was obliterated completely. ICA: internal carotid artery

Table 2 Comparison of recurrent and non-recurrent cases

Factor	Recurrence	Non-recurrence	p Value
Age (~60: 61–75: 76~)	6: 3: 1	35: 26: 27	0.329
Hunt–Kosnik grade (I–II: IV–V)	6: 4	71: 17	0.131
Aneurysm location* (pIC: dIC: Acom: VBA: Others)	3: 1: 4: 2: 0	4: 32: 28: 19: 5	0.029
Aspect ratio (~1.5: 1.6–2: 2.1~)	4: 1 :5	25 :32 30	0.238
Neck diameter (~2 mm: 2.1–4: 4.1~)	1: 5: 4	16: 46: 26	0.831
Maximum aneurysm diameter (~5 mm: 5.1–10: 11~)	1: 6: 3	24: 48: 16	0.418
Volume embolization ratio (~20%: 21–30: 31~)	2: 5: 3	12: 43: 32	0.838
RR at initial embolization* (DF: NR: CO)	0: 7: 3	2: 20: 66	0.0065
Intraoperative complication (thrombus: others: No)	0: 1: 9	8: 5: 75	0.547
RR at day 7–11 DSA* (DF: NR: CO)	2: 7: 1	1: 16: 71	<0.0001
RR deterioration at day 7–11 DSA* (Yes: No)	9: 1	1: 86	<0.0001
Glasgow Outcome Scale (GR and MD: SD and VS)	10: 0	66: 22	0.0726

* p <0.05. Acom: anterior communicating artery; CO: complete obliteration; D: death; DF: dome filling; dIC: distal internal carotid artery (C1); GR: good recovery; MD: moderately disabled; NR: neck remnant; pIC: proximal intradural carotid artery (C3~2); RR: Raymond–Roy classification; SD: severely disabled; VBA: vertebra-basilar artery; VS: vegetative state

Table 3 Logistic regression analysis of recurrence of aneurysm

Factor	Degrees of freedom	Likelihood-ratio chi-square test	p Value (prob >chiSq)
Aneurysm location (pIC: dIC: Acom: VBA: Others)	4	7.529	0.1104
RR at initial embolization (DF: NR: CO)	2	2.911	0.2333
RR at day 7–11 DSA* (DF: NR: CO)	2	1.726	0.4219
Increased contrast medium in aneurysm at day 7–11 DSA (Yes: No)	1	17.79	<0.0001

Acom: anterior communicating artery; CO: complete obliteration; dIC: distal internal carotid artery (C1); DF: dome filling; NR: neck remnant; pIC: proximal intradural carotid artery (C3~2); RR: Raymond–Roy classification; VBA: vertebra-basilar artery

A proximal ICA aneurysm, Raymond–Roy classification at initial embolization and at day 9 ± 2, and increased contrast medium in the aneurysm at postoperative DSA during day 9 ± 2 were statistically related to the recurrence of the aneurysm (**Table 2**). Aspect ratio, aneurysm size, VER, and intraoperative complication did not correlate with aneurysm recurrence (**Table 2**).

Logistic regression analysis showed that increased contrast medium in the aneurysm at day 9 ± 2 was statistically related with aneurysm recurrence (**Table 3**). Deterioration of the Raymond–Roy classification during day 9 ± 2 was not related with aneurysm recurrence.

Recurrence or retreatment of an aneurysm did not influence the Glasgow Outcome Scale. In those 10 recurrent cases, 8 cases achieved good recovery (GR) and 2 cases achieved moderately disabled (MD). No recurrent case was later repeated.

Discussion

We report for the first time that recurrence of an embolized ruptured aneurysm can be estimated by postoperative DSA at day 9 ± 2 while ruptured proximal ICA aneurysms exhibited significant recurrence. A chronological increase in contrast medium in the aneurysm is important in the follow-up of the embolized ruptured cerebral aneurysm. In our study, the Raymond–Roy classification was not determined to be a significant factor in aneurysm recurrence by multivariate analysis.

After aneurysm rupture, enhancement of platelet sensitivity and elevation of the von Willebrand factor take place due to endothelial injury.[13,14] Antiplatelet-aggregation activity is significantly activated in human SAH patients and also in an animal SAH model.[15,16] Thrombus formation readily occurs on the surface of foreign material. Physicians cannot observe the cross-section of an aneurysm neck from inside the vessel, so they cannot judge whether the center of the neck has a tight coil mass or not. Even if the center of the aneurysm neck has a loose coil, obliteration that appears complete but is not (false) may occur during the acute phase of SAH. Abnormal coagulation conditions improve as of several days after the SAH, allowing us to judge the true obliteration status of an aneurysm. A follow-up DSA at day 9 ± 2 can therefore be used to evaluate the embolized state of an aneurysm.[13,15] Moreover, angiographical vasospasm did not influence the occlusion status of aneurysm in our

series. We can estimate aneurysm recurrence with postoperative DSA at day 9 ± 2 after the ictus. We can also manage suitable imaging follow-up and re-treatment of the aneurysm from the acute period of SAH onward. Re-treatment does not influence the outcome of SAH. We should carry out re-treatment of a recurrent aneurysm to avoid re-rupture of the aneurysm. A staged obliteration strategy using either stents or flow diversion can then be selected.

An MRA is a candidate as an alternative to DSA imaging. But metallic artifacts such as stents in particular and also cisternal blood reduce the quality of an MRA. DSA is therefore superior to MRA in diagnosing an aneurysm neck remnant during the acute period.

In both International Subarachnoid Aneurysm Trial (ISAT) and Barrow Ruptured Aneurysm Trial (BRAT), rebleeding and/or retreatment within 1 year of the first treatment were 5%–6.9%.[17,18] Aneurysm retreatment decreased markedly 1 year after the initial treatment.[1,2] In our study, there was no need to undertake any re-treatment after 1 year post-treatment. Only one case in this series exhibited rebleeding 5 days after the initial coiling. This case was treated during vasospasm and a precise evaluation of the aneurysm occlusion could not be done at the first session. Complete obliteration at the first coiling is very important.

A small number of papers have reported recurrence and / or retreatment of ruptured cerebral aneurysm after coiling in relation to the location of the aneurysm.[3–6] Although the long-term stability of aneurysm occlusions has improved over time, the rate of recurrence differs with various aneurysm locations. High recurrence rates for an IC-PC aneurysm and a BA aneurysm have been reported, but no report has described a high recurrence rate for a coiled ruptured proximal IC aneurysm.[3–6] Several researchers have reported a relatively low complete obliteration rate and a high recurrence rate for proximal IC aneurysms.[19–21] Those reports include mainly unruptured aneurysms and focused only on proximal IC aneurysms.

The number of ruptured proximal IC aneurysm cases in our series is small, but the recurrence rate is high in this portion. A kinked parent ICA inhibits catheter manipulation. All physicians should achieve complete obliteration of the aneurysm using catheter shaping and adjuvant techniques. Ours is the first report on the high recurrence rate of coiled ruptured proximal IC aneurysms.

Our result shows that the aneurysm size or VER does not correlate with aneurysm recurrence. Aneurysm size and VER are recognized as relevant for successful treatment.[22–24] Our VER is higher relative to previous reports. Recently available very soft coils with less kick back have increased the VER. Adjuvant methods also aid in inserting the coil into the aneurysm dome. Our results are thus different from previous reports.

Conclusion

An increase in contrast medium in the aneurysm on postoperative DSA at day 9 ± 2 is predictive of the recurrence of an embolized ruptured aneurysm and ruptured proximal ICA aneurysms exhibited significant recurrence.

Acknowledgment

We thank Mark Inglin (University of Basel) for his editorial assistance.

Disclosure Statement

The authors declare no conflict of interest.

References

1) Molyneux AJ, Birks J, Clarke A, et al: 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: 691–697.
2) Spetzler RF, McDougall CG, Zabramski JM, et al: Ten-year analysis of saccular aneurysms in the Barrow Ruptured Aneurysm Trial. *J Neurosurg* 2020; 132: 771–776.
3) Corns R, Zebian B, Tait MJ, et al: Prevalence of recurrence and retreatment of ruptured intracranial aneurysms treated with endovascular coil occlusion. *Br J Neurosurg* 2013; 27: 30–33.
4) Gallas S, Januel AC, Pasco A, et al: Long-term follow-up of 1036 cerebral aneurysms treated by bare coils: a multicentric cohort treated between 1998 and 2003. *AJNR Am J Neuroradiol* 2009; 30: 1986–1992.
5) Mortimer AM, Marsh H, Klimczak K, et al: Is long-term follow-up of adequately coil-occluded ruptured cerebral aneurysms always necessary? A single-center study of recurrences after endovascular treatment. *J Neurointerv Surg* 2015; 7: 373–379.
6) Raymond J, Guilbert F, Weill A, et al: Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. *Stroke* 2003; 34: 1398–1403.
7) Shimamura N, Naraoka M, Matsuda N, et al: Use of preprocedural, multiple antiplatelet medications for coil

embolization of ruptured cerebral aneurysm in the acute stage improved clinical outcome and reduced thromboembolic complications without hemorrhagic complications. *World Neurosurg* 2020; 133: e751–e756.

8) Mascitelli JR, Moyle H, Oermann EK, et al: An update to the Raymond-Roy occlusion classification of intracranial aneurysms treated with coil embolization. *J Neurointerv Surg* 2015; 7: 496–502.
9) Ujiie H, Tachibana H, Hiramatsu O, et al: Effects of size and shape (aspect ratio) on the hemodynamics of saccular aneurysms: a possible index for surgical treatment of intracranial aneurysms. *Neurosurgery* 1999; 45: 119–129; discussion 129-130.
10) Satoh K, Matsubara S, Hondoh H, et al: Intracranial aneurysm embolization using interlocking detachable coils. Correlation between volume embolization rate and coil compaction. *Interv Neuroradiol* 1997; 3 Suppl 2: 125–128.
11) Roy D, Milot G, Raymond J: Endovascular treatment of unruptured aneurysms. *Stroke* 2001; 32: 1998–2004.
12) Jennett B, Bond M: Assessment of outcome after severe brain damage. *Lancet* 1975; 1: 480–484.
13) Fujii Y, Takeuchi S, Sasaki O, et al: Serial changes of hemostasis in aneurysmal subarachnoid hemorrhage with special reference to delayed ischemic neurological deficits. *J Neurosurg* 1997; 86: 594–602.
14) Nina P, Schisano G, Chiappetta F, et al: A study of blood coagulation and fibrinolytic system in spontaneous subarachnoid hemorrhage. Correlation with Hunt-Hess grade and outcome. *Surg Neurol* 2001; 55: 197–203.
15) Ohkuma H, Ogane K, Fujita S, et al: Impairment of antiplatelet-aggregating activity of endothelial cells after experimental subarachnoid hemorrhage. *Stroke* 1993; 24: 1541–1545; discussion 1545-1546.
16) Ohkuma H, Suzuki S, Kimura M, et al: Role of platelet function in symptomatic cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Stroke* 1991; 22: 854–859.
17) McDougall CG, Spetzler RF, Zabramski JM, et al: The Barrow Ruptured Aneurysm Trial. *J Neurosurg* 2012; 116: 135–144.
18) Molyneux A, Kerr R, Stratton I, 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: 1267–1274.
19) Boet R, Wong GK, Poon WS, et al: Aneurysm recurrence after treatment of paraclinoid/ophthalmic segment aneurysms–a treatment-modality assessment. *Acta Neurochir (Wien)* 2005; 147: 611–616; discussion 616.
20) D'Urso PI, Karadeli HH, Kallmes DF, et al: Coiling for paraclinoid aneurysms: time to make way for flow diverters? *AJNR Am J Neuroradiol* 2012; 33: 1470–1474.
21) Wang Y, Li Y, Jiang C, et al: Endovascular treatment of paraclinoid aneurysms: 142 aneurysms in one centre. *J Neurointerv Surg* 2013; 5: 552–556.
22) Chalouhi N, Dumont AS, Hasan D, et al: Is packing density important in stent-assisted coiling? *Neurosurgery* 2012; 71: 381–386; discussion 386-387.
23) Huang DZ, Jiang B, He W, et al: Risk factors for the recurrence of an intracranial saccular aneurysm following endovascular treatment. *Oncotarget* 2017; 8: 33676–33682.
24) Sluzewski M, van Rooij WJ, Slob MJ, et al: Relation between aneurysm volume, packing, and compaction in 145 cerebral aneurysms treated with coils. *Radiology* 2004; 231: 653–658.