EDITOR'S CHOICE

Long-term effects of antiplatelet drugs on aneurysm occlusion after endovascular treatment

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ABSTRACT

Background The rates of recanalization and reinterventions after endovascular treatment (EVT) of intracranial aneurysms are unknown. Various risk factors have been suggested including the configuration of the aneurysm and the endovascular technique. Recently, an increasing number of patients have received antiplatelet (AP) drugs periprocedurally, possibly inhibiting early thrombus formation.

Objective To assess the impact of AP drugs on the rate of recurrence and reintervention.

Methods Patients treated at our center were entered into a prospectively conducted database. Those with at least one follow-up angiogram 6 months after EVT were selected for the study. The role of AP medication was assessed by statistical analysis.

Results 292 patients with 314 aneurysms (206 ruptured) were included. The median follow-up time was 18 months. 129 (41%) were treated with APs (70 with acetylsalicylic acid (ASA), 10 with clopidogrel and 48 with both). 107 angiographic aneurysm recurrences were noted and 61 aneurysms were retreated at least once. In a multivariate model only aneurysm size, initially incomplete occlusion and the length of follow-up were significant predictors ($p<0.05$). No correlation was found between AP administration and recurrences or reinterventions. Interestingly, patients receiving ASA alone were retreated less often (OR 0.187, 95% CI 0.061 to 0.572, $p=0.003$).

Conclusion AP administration is not associated with an increased rate of aneurysm recurrence or reintervention; ASA even seemed to have some beneficial effect. However, confounding factors may include the lack of standardized indications for AP and the small number of patients in the series. A prospectively conducted study is warranted to further clarify the role of AP medication after EVT.

INTRODUCTION

Endovascular treatment (EVT) of intracranial aneurysms is effective and it has been suggested that the outcome after EVT might be even better than after surgery in patients with acute subarachnoid hemorrhage (SAH).[1] Furthermore, EVT is an established therapeutic option in unruptured aneurysms.[2–4] In general, EVT is considered safe as the risk of rebleeding seems to be very low (0–4.9%)[1 3–18] compared with surgical clipping (0–1.2%).[1 7 10] Nevertheless, incomplete aneurysm occlusion and recurrences are more frequent than with surgery. Although the clinical relevance of pure angiographic aneurysm recurrence is not yet clear, in general it is considered as a potential risk factor for future aneurysm rupture.[19] As a consequence, a significant proportion of aneurysms treated with EVT require repeated interventions, either endovascularly or surgically.

Despite recanalization rates of up to 20% or more, little is known about the contributing factors. Suggestions include aneurysm-specific factors such as size, configuration, location, history of rupture or the neck-to-dome ratio and EVT-associated factors such as the initial occlusion rate.[2 3 5 6 8 9 12 13 16 17 20 21] In this study we have focused on the use of antiplatelet (AP) medications such as aspirin (ASA) or clopidogrel (CLOP) after EVT and their influence on the rate of aneurysm recurrence and retreatment.

METHODS

Patient population

All patients admitted to our institution between April 1999 and January 2010 with intracranial aneurysms were entered into a prospectively collected database. Patients treated by EVT with at least one follow-up angiogram 6 months later were included in the study and their data reviewed.

Endovascular treatment

Each aneurysm was assessed by an interdisciplinary neurovascular team and, based on the characteristics of the individual aneurysm and the clinical condition of the patient, the best treatment (EVT or surgical clipping) was chosen.[22] After SAH, treatment within 48 h was targeted. After aneurysm obliteration, all patients were admitted to the neurosurgical intensive care unit.

EVT was performed under general anesthesia after a bolus administration of 5000 IU heparin. Various types of platinum coils were used during the treatment period. Aneurysms were packed with coils as densely as possible.

In selected patients the balloon remodeling technique was applied and/or an endovascular stent was placed. According to previous published series, the occlusion rate was documented and categorized as: (1) complete; (2) residual filling of the aneurysm neck; or (3) residual filling of the dome.[15 20]

Application of APs

Heparinization was routinely continued for 24–48 h after EVT (goal: activated clotting time 1.5× normal). AP medication was applied as recommended by the neurointerventionalist. The indications were broad surface between coils and parent vessel, coil protrusion into the parent vessels or thromboembolic events during the procedure. In

SAH requiring ventricular drainage or possible further surgical intervention, surgical aneurysm obliteration was preferred when APs would have been required as judged by the neurointerventionalist. Exceptions were only made in the posterior circulation as, for example, in complex basilar tip aneurysms. The duration of treatment with APs was continued as recommended by the neurointerventionalist, usually for at least 2 weeks.

In patients undergoing stent placement, 75 mg CLOP and 100 mg ASA were given for 3 months. In general, patients received 75 mg CLOP and 100 mg ASA daily for 4–5 days before EVT. If this was not possible in, for example, ruptured aneurysms, patients received a single dose of 250 mg ASA intravenously and a heparin bolus of 100 IU/kg during the procedure and a loading dose of 600 mg CLOP as soon as possible. With the introduction of glycoprotein IIb/IIIa inhibitors for emergency cases, a bolus of 0.4 μg/kg tirofiban was given before stent placement followed by 0.1 μg/kg. Tirofiban was discontinued after a loading dose of 600 mg CLOP.

Some patients received AP medication due to underlying medical conditions such as ischemic heart disease.

Follow-up evaluation

We routinely perform conventional angiography 6 months after EVT. The digital subtraction technique was used and multiple projections including 3D-rotational angiography were obtained to evaluate residual aneurysm perfusion. If digital subtraction showed an unchanged result, MR time-of-flight angiography was chosen for further follow-up at 3–12-month intervals as recommended in various studies.[23–26] If there was a suspicion of a relevant change in the occlusion rate, a conventional angiogram was obtained to evaluate further treatment indications.

Aneurysm obliteration was assessed based on strict anatomical considerations and compared with the initial EVT result. It was categorized according to the classification originally proposed by Raymond *et al* as: (1) unchanged occlusion of the aneurysm without recanalization including the aneurysm neck or improved aneurysm obliteration compared with the initial EVT; (2) recanalization of any portion of the aneurysm neck without opacification of the original aneurysm sac; or (3) any recanalization with contrast filling within the dome.[20] Recurrence was thereby defined as any increase in contrast opacification within the aneurysm or its neck compared with the last series of EVT.

In cases of aneurysm recurrence, two groups were distinguished: (1) patients in whom a small angiographic recurrence was noted but who were considered to be protected from rebleeding and, in general, retreatment was not possible; these patients were observed with close follow-up imaging; and (2) patients with larger recurrences in whom reintervention (either surgically or endovascularly) was undertaken whenever theoretically feasible using a method chosen by the interdisciplinary neurovascular team. We consider that aneurysm recurrence and retreatment are different endpoints and require separate analysis as the clinical relevance for the patient is different. We therefore summarized all angiographic recurrences as one group and defined reintervention as a separate endpoint.

The interval (in months) between treatment and the first follow-up angiogram showing recurrence was noted. Hemorrhagic events due to rupture of the treated aneurysms were recorded.

Statistical analysis

Statistical analysis was performed using the SPSS software Version 17.0.0 (SPSS Inc). When a patient had more than one aneurysm, they were considered independently for the purpose of statistical analysis. Aneurysm size and time were studied as continuous variables and aneurysm size was also analyzed by groups (≥10 mm).

For patients grouped according to aneurysm recurrence or retreatment, history of aneurysm rupture, location at an anatomical bifurcation (internal carotid artery (ICA) bifurcation, middle cerebral artery (MCA) bifurcation or basilar tip vs sidewall aneurysm), gender, and initial obliteration rate (dichotomized as complete or incomplete) were evaluated for statistically significant differences between the groups using a χ^2 test. Patient age and size of the aneurysm were compared using the Mann–Whitney U test.

Univariate analysis was performed to evaluate the effect of AP medication on recurrence and retreatment. The rates were separately assessed in the subgroups according to aneurysm size (using 10 mm as a threshold), location (either anatomically as bifurcation or within the circle of Willis as anterior circulation (including posterior communicating artery (PCom) aneurysms[3 8 11]) vs posterior circulation), history of aneurysm rupture, initial occlusion rate, use of a stent and administration of APs (categorized as none, CLOP alone, ASA alone or both) with the χ^2 test. Age, aneurysm size and duration of follow-up as continuous variables were compared using the Mann–Whitney U test. Finally, a stepwise logistic regression analysis was performed to determine risk factors associated with angiographic recurrence and retreatment, respectively. Probability values <0.05 were considered statistically significant.

RESULTS

Patient population

From 1999 to 2010, 632 patients (72% with a ruptured aneurysm) were treated by EVT at our center. Two hundred and ninety-two patients with 314 treated aneurysms fulfilled the inclusion criteria. Patients did not undergo follow-up examinations mainly due to an unfavorable measure on the Glasgow Outcome Scale (GOS) or follow-up at other institutions. Other reasons included patient refusal or patients lost to follow-up.

Two hundred and six aneurysms (65.6%) were ruptured: 102 of the patients with SAH presented with World Federation of Neurosurgeons Scale (WFNS) grade 1 (49.5%), 35 with WFNS grade 2 (17.0%), 18 with WFNS grade 3 (8.7%), 14 with WFNS grade 4 (4.4%) and 37 with WFNS grade 5 (18.0%).

The aneurysm distribution was: 81 anterior communicating artery complex (Acom), 6 distal anterior cerebral artery, 112 ICA (including 55 aneurysms at the origin of the PCom), 26 MCA, 65 basilar artery (BA), 8 vertebral artery (VA), 13 posterior inferior cerebellar artery (PICA) and 3 posterior cerebral artery (PCA) (table 1). The aneurysm diameter ranged from 2 to 29 mm (median 6, IQR 4).

Initially, a stent was placed in 26 cases (8.2%) and the remodeling technique was used in 14 cases (4.4%). At the end of the procedure 174 of 314 aneurysms were totally occluded (55.4%) whereas residual contrast filling of the aneurysm neck or dome was noted in 123 (39.2%) and 17 (5.4%) aneurysms, respectively. There was no significant difference between the occlusion rate of ruptured aneurysms (complete occlusion in 119 (57.8%), residual neck in 76 (36.9%), residual dome in 11 (5.3%)) and unruptured aneurysms (complete occlusion in 55 (50.5%), residual neck in 48 (44.0%), residual dome in 6 (5.5%); p=0.497).

Follow-up angiographic analysis

Median follow-up was 18 months (range 6–158, IQR 30). In 207 aneurysms the initial result was stable (65.9%). In 107

Table 1 Distribution of aneurysms and treatment details

Aneurysm location	n	Ruptured	AP medication	Recurrence/retreatment	Initial occlusion
ACA	87	n=72 (82.8%)	ASA n=15 CLOP n=1 Both n=4	n=22 (25.3%)/n=15 (17.2%)	Complete n=49 Res. neck n=33 Res. dome n=5
ICA	112	n=55 (49.1%)	ASA n=32 CLOP n=4 Both n=20	n=34 (30.4%)/n=15 (14.4%)	Complete n=59 Res. neck n=48 Res. dome n=5
MCA	26	n=15 (57.7%)	ASA n=6 CLOP n=2 Both n=3	n=10 (38.5%)/n=8 (30.8%)	Complete n=14 Res. neck n=11 Res. dome n=1
BA	65	n=44 (67.7%)	ASA n=3 CLOP n=3 Both n=15	n=35 (53.8%)/n=19 (29.2%)	Complete n=38 Res. neck n=22 Res. dome n=5
Other	24	n=20 (83.3%)	ASA n=4 CLOP n=0 Both n=6	n=6 (25.0%)/n=4 (16.7%)	Complete n=14 Res. neck n=9 Res. dome n=1
Total	314	n=206 (65.5%)	ASA n=70 CLOP n=10 Both n=48	n=107 (34.1%)/n=61 (19.4%)	Complete n=174 Res. neck n=123 Res. dome n=17

ACA, anterior cerebral artery including anterior communicating artery; AP, antiplatelet; ASA, acetyl salicyclic acid; BA, basilar artery; CLOP, clopidogrel; ICA, internal carotid artery including posterior communicating artery; MCA, middle cerebral artery; res, residual.

aneurysms (34.0%) recanalization was noted. Sixty aneurysms were retreated: 51 underwent at least one additional EVT and 10 aneurysms were clipped. In 50 aneurysms one additional procedure was sufficient, in seven aneurysms two interventions were needed and four aneurysms required three additional interventions. The median interval to the second treatment was 8 months (range 1–108, IQR 11).

Recanalization was most often noted at the BA (35 of 65 aneurysms, 53.8%) followed by the MCA (10 of 26 aneurysms, 38.5%). Retreatment was most often performed at the MCA (8 of 26 aneurysms, 30.8%) followed by the BA (19 of 65 aneurysms, 29.2%, table 1). Aneurysms ≥10 mm had significantly higher rates of recurrence and retreatment (p=0.003 and p=0.002, respectively, tables 2 and 3). Furthermore, recurrence was statistically more likely in initially incompletely occluded aneurysms (p<0.001) and aneurysms of the posterior circulation (p=0.004). The rate of recurrence also increased with the length of follow-up (p=0.004). Similar risk factors were identified for aneurysm retreatment.

The rate of recurrence or retreatment was not significantly different between ruptured and unruptured aneurysms (p=0.764 and p=0.544, respectively) and was not affected by gender (p=0.190 and p=0.465) or age (p=0.166 and p=0.499).

Impact of AP medication

One hundred and seventy-eight patients (60.9%) received no AP medication (186 aneurysms, 59.0%), 66 patients (22.6%) were treated with ASA only (70 aneurysms, 22.2%), 9 patients (3.1%) received CLOP only (10 aneurysms, 3.2%) and 39 patients (13.4%) received both (48 aneurysms, 15.2%) (table 1). Patients were treated with AP medication for 1–>48 weeks after EVT (median 12.0). Patients with ruptured aneurysms were significantly less likely to receive AP medication, as expected owing to the management at our institution (30 (14.6%) vs 40 (36.7%), p<0.001; table 4). Furthermore, there was a statistically significant difference in the aneurysm size of patients who did and did not receive AP treatment, those with larger aneurysms receiving AP medication more often (p=0.001).

In general the administration of AP medication had no impact on aneurysm recurrence (table 2). In the subgroup analysis the incidence of recanalization was not influenced by the administration of ASA only (p>0.05) compared with the other AP groups or all other patients. However, recanalization was more frequent in the group of patients treated with ASA + CLOP (p=0.028). Thirteen of these patients had a stent and thus were treated with ASS + CLOP whereas 10 patients did not have a stent but received combined AP medication.

Table 2 Logistic regression analysis for aneurysm recurrence

	Logistic regression (stepwise, forward)			χ^2 Test	Mann–Whitney U test
Effect	p Value	OR	95% CI	p Value	p Value
Antiplatelets	0.697			0.412	
ASS only	0.715			0.596	
ASS + CLOP	0.155			0.028 *	
Age	0.422				0.166
Gender	0.320			0.190	
Aneurysm size	0.026*	1.082	1.009 to 1.159		0.907
Ruptured aneurysm	0.854			0.764	
Aneurysm ≥10 mm	0.017*	2.041	1.138 to 3.659	0.003*	
Anatomic bifurcation	0.601			0.043*	
Posterior circulation	0.011*	2.032	1.175 to 3.513	0.004*	
Initial incomplete occlusion	<0.001*	2.813	1.702 to 4.648	<0.001*	
Duration of follow-up	0.013*	1.013	1.003 to 1.024		0.004*
Stent	0.290			0.074	

*Significant values. For the subgroups ASS only, ASS + CLOP and aneurysm size ≥10 mm, separate logistic regression models were calculated, respectively.
ASA, acetyl salicyclic acid; CLOP, clopidogrel.

Table 3 Logistic regression analysis for aneurysm retreatment

Effect	Logistic regression (stepwise, forward) p Value	OR	95% CI	χ^2 Test p Value	Mann–Whitney U test p Value
Antiplatelets	0.254			0.262	
ASS only	0.003*	0.187	0.061 to 0.572	0.001*	
ASS + CLOP	0.404			0.024*	
Age	0.401				0.499
Gender	0.722			0.533	
Aneurysm size	0.022*	1.095	1.017 to 1.042		0.517
Ruptured aneurysm	0.549			0.544	
Aneurysm ≥10 mm	0.007*	2.382	1.272 to 4.459	0.002	
Anatomic bifurcation	0.670			0.161	
Posterior circulation	0.352			0.061	
Initial incomplete occlusion	0.001*	2.733	1.473 to 5.069	<0.001*	
Duration of follow-up	<0.001*	1.030	1.017 to 1.042		<0.001*
Stent	0.235			0.127	

*Significant values. For the subgroups ASS only, ASS + CLOP and aneurysm size ≥10 mm, separate logistic regression models were calculated, respectively.
ASA, acetyl salicyclic acid; CLOP, clopidogrel.

Of the 61 retreated aneurysms, 40 had no AP medication (21.5% of patients without AP), 15 received ASA + CLOP, two received CLOP only and four received ASA only (31.3%, 20.0% and 5.7% of the specific treatment groups, respectively). AP medication did not increase the risk of a second intervention (p=0.262). No additional risk of further treatment was found in the statistical analysis for the specific groups but, for the ASA only group, the rate of additional treatment was significantly lower than in all the other patients (OR 0.200, 95% CI 0.070 to 0.572, p=0.001) and compared with patients without AP (OR 0.221, 95% CI 0.076 to 0.644, p=0.003, table 3).

Logistic regression analysis

Two different endpoints were used for the logistic regression analysis (stepwise model, forward): aneurysm recurrence and aneurysm retreatment (see tables 2 and 3). Aneurysm recurrence was more likely for initially incompletely occluded aneurysms, larger aneurysms (either median size or dichotomized using a cut-off value of 10 mm) and aneurysms located in the posterior circulation. Furthermore, the likelihood of aneurysm recurrence increased with the length of follow-up.

Significant factors for an additional treatment were aneurysm size (median and cut-off ≥10 mm) and initially incomplete aneurysm occlusion; the administration of ASA only was associated with a statistically significant reduction in the reintervention rate. As for aneurysm recurrence, the likelihood of aneurysm retreatment increased with the length of follow-up.

Late rebleeding

Three patients (1.02%) had late rebleeding (one MCA bifurcation and two basilar tip aneurysms), only one of which (BA) was initially completely occluded. In the other two, residual filling of the neck and dome, respectively, occurred.

The rebleeding occurred 5, 84 and 102 months after the first treatment. Initially no patient received AP medication but, at the time of rebleeding, one patient was treated with 300 mg ASA daily due to recurrent ischemic stroke as well as myocardial infarction. Another patient was treated with CLOP after a previous ischemic stroke. After rebleeding (WFNS grade 5 in two and WFNS grade 4 in one case) the outcome was poor (GOS 1 in two patients and GOS 2 in one patient).

DISCUSSION

In this retrospective analysis we assessed the effect of AP medication after EVT on the long-term stability of aneurysm occlusion. The use of AP medication did not increase the risk of aneurysm recurrence or retreatment. Indeed, ASA might even have some protective effect on major recurrences requiring reintervention.

As the significance of the recurrence of small angiographic aneurysms is unclear, we divided our analysis into (1) overall angiographic aneurysm recurrence and (2) aneurysm retreatment as we suspect that aneurysm recurrence alone may not be a significant endpoint. Angiographic recurrence may be only a small increase in contrast opacification compared with the initial EVT and may be due to some degree of coil compaction. The significance of these small recurrences for the risk of future aneurysm rupture is not known but seems to be very small and reintervention is usually technically not possible. It remains unclear if such recurrences present any risk to the patient. In general, close follow-up of these aneurysms is performed.[2 13 15]

Table 4 Baseline demographic data for all included patients and subgroups of patients with and without antiplatelet (AP) drugs

	All n (%)	No AP n (%)	With AP n (%)	p Value
Age (mean±SD)	50.34±11.41	49.41±11.16	51.68±11.67	0.075
Male sex	91 (29.0)	62 (32.8)	30 (23.4)	0.072
Anatomic bifurcation	100 (31.8)	53 (28.5)	47 (36.7)	0.124
Size in mm (median)	6.35	6.00	7.00	0.001*
Ruptured aneurysms	206 (65.6)	155 (83.3)	51 (37.5)	0.000*
Posterior circulation	88 (28.0)	48 (25.8)	40 (31.3)	0.291
Length of follow-up (median)	18.00	20.00	17.50	0.130

*Statistically significant differences. The Mann–Whitney U test was used for age, aneurysm size and length of follow-up and the χ^2 test was used for the other variables.

On the other hand, once the recurrence is big enough technically to allow reintervention, the risk of future aneurysm rupture may also increase so attempts at retreatment are needed in these cases. Reintervention may be associated with a new permanent deficit for the patient, although the risk of this is very low.[4 6 9 13 16] To determine whether there is a significant difference between the groups, we divided our analysis between the incidence of (1) overall angiographic recurrence and (2) clinically relevant recurrences leading to a reintervention.

Various risk factors for aneurysm recurrence have been identified. In this study we confirm an increased risk of retreatment in large and initially incompletely occluded aneurysms. Our results lie within the range reported in other series (table 5). Furthermore, the detection of aneurysm recurrence and retreatment both increased with the length of follow-up, as noted previously.[2]

The limitations of our study are its retrospective nature and the small numbers of patients in the various subgroups which limit the statistical power. Many patients did not have follow-up imaging, which may be associated with the high percentage of patients with SAH. In unfavorable outcomes, angiography is often omitted due to a lack of consequences. This may lead to a selection bias, with reinterventions over-represented as patients were informed about the importance of follow-up imaging, especially in incompletely occluded unruptured aneurysms. Furthermore, indications for the retreatment of a recurrent aneurysm need to be better defined as the natural history and clinical significance of a residual aneurysm neck remain unclear. Finally, the different types of coils used during the observed period may have an effect on the recurrence rate which cannot be determined, although recent studies found no evidence for the superiority of one coil material over others.[27 28]

Although significantly more patients with unruptured aneurysms received ASA, we think that this can be ignored as there was no difference in the occlusion rates or in the reintervention rates between those with ruptured and unruptured aneurysms. It is not clear if ruptured aneurysms have a higher recanalization rate; some studies[2 17 21] found an associated risk while others did not.[6 8] It has to be borne in mind that the selection of aneurysms for EVT is different in unruptured aneurysms, and aneurysms appearing to be unfavorable for EVT are more likely to be treated surgically whereas, in patients with SAH, EVT is often preferred.

Table 5 Summary of recent studies investigating the long-term stability after endovascular treatment

Study	Initially complete occlusion (%)	Recanalization (%)	Retreatment (%)	Rebleeding (%)
Cognard *et al*[21]	56	13.5	3.4	–
Murayama *et al*[3]	55	20.9	–	1.6
Raymond *et al*[2]	35.9	33.6	10.9	–
Sluzewski *et al*[14]	80.3	–	–	1.6
Henkes *et al*[16]	63.7	–	23.6	2.2
CARAT Investigators[7]	–	–	19.4	0.3
Aikawa *et al*[18]	–	–	9.7	2.6
Grunwald *et al*[6]	85	22.2	7.8	0
Nguyen *et al*[17]	39.7	33.6	13.4	2.6
Pandey *et al*[11]	87.8	24.5	4.9	1.1
Holmin *et al*[4]	54.3	15.7	15.3	0.3
Renowden *et al*[13]	–	–	8.0	1.5
Gallas *et al*[8]	70.5	18.1	6.7	0.5
Willinsky *et al*[15]	43	20.3	–	2.1
Present study	55.2	34.0	19.4	1.0

Role of AP medication

ASA and other anticoagulants are frequently used after EVT since it has been shown that they reduce periprocedural thromboembolism.[29 30] However, no systematic guidelines exist for their administration so a variety of anticoagulation regimes are used. Nevertheless, the long-term effect of these drugs on aneurysm occlusion is unknown. As the mechanisms of recanalization are not fully understood and the resulting risk of haemorrhage is not clearly defined, long-term follow-up after EVT is necessary.[2]

After EVT, endothelialization of the defect between the parent vessel lumen and coil package is needed to guarantee permanent occlusion of the aneurysm. Histopathological studies show that endotheliazation is frequently incomplete, especially if the space between two coil loops is larger than the diameter of one coil.[31]

Development and maturation of a thrombus after coil placement is important for stable aneurysm occlusion. Organized clot anchors the coils in place and is replaced by fibrous tissue between the coil loops creating a barrier for inflow of blood or coil compaction.[3 31–33]

The presence of flow in incompletely occluded or recanalized aneurysms prevents progressive thrombosis, thrombus organization and intra-aneurysmal scarring.[11 33] Thus, the initial advantage of periprocedural anticoagulation (fewer thromboembolic events) may later become a disadvantage with regard to permanent aneurysm occlusion.

In our study APs were not associated with a higher reintervention rate. This is surprising as the aneurysms treated with APs were significantly larger than those not treated with APs and aneurysm size is a known risk factor for recurrence. Only patients receiving a combination of ASA and CLOP showed an increased rate of recanalization, although the difference was not significant in the multivariate analysis. Interestingly, most of these patients were treated with a stent. In general, stents are used to treat more complex aneurysms such as those with a wide neck. Our study therefore does not support the results of Piotin *et al* who found fewer recurrences after stent placement.[34] This may be because the initial advantages of a stent are later overcome by the lack of thrombus formation due to the combined platelet inhibition.

On the other hand, patients receiving ASA alone had a significantly lower risk of aneurysm recurrence requiring reintervention. The interpretation of this result is difficult. In an experimental study ASA did not affect thrombus organization in the aneurysm.[32] In the clinical setting the lack of strict indications for the administration of ASA seems to be important. First, one might argue that aneurysms treated with ASA alone are less complex, while complex aneurysms are more frequently treated with stents requiring ASA and CLOP, leading to different reintervention rates. Second, ASA is often administered to patients with aneurysms with a broad surface or protrusion of coil material into the parent artery. This might occur more often in aneurysms treated more aggressively by the neurointerventionalist trying to achieve maximal aneurysm occlusion. In wide-necked aneurysms in particular this strategy might be useful, leading to better long-term stability.[3] However, we could not prove this hypothesis statistically as the rate of complete occlusion in patients treated with ASA did not differ from those not treated with ASA. Finally, ASA might inhibit platelet activation otherwise triggering an inflammatory reaction with

secretion of molecules that may favor recanalization or recruitment of cells involved in recanalization after EVT.[35]

CONCLUSIONS

In this study AP medication did not increase the risk of aneurysm recurrence or reintervention. Indeed, ASA alone was associated with a lower reintervention rate. As the indications for the administration of ASA are not standardized and the numbers in our study were limited, further prospective studies are needed to confirm our findings.

Competing interests None.

Contributors JP: conception and design; JP, EG: acquisition of data; JP, JB: analysis and interpretation of data; JP: drafting the article; JB, VS, HV: critically revising the article.

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