Endovascular Treatment of Cerebral Aneurysms in Relation to Their Parent Artery Wall: a Single Center Study

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SUMMARY – *We report our two-year experience in the endovascular treatment of brain aneurysms in relation to their parent artery wall. We prospectively recorded patients with intracranial aneurysms (107 ruptured - 38 unruptured) treated with coiling during a two-year period: 145 patients, 94 females and 51 males - mean age 56 years. The aneurysms were divided into side-wall (A) and bifurcation (B) groups. A total occlusion rate was noted in post-embolization angiograms in 101 aneurysms (70%) with a morbidity of 4%. No angiographic recurrence arose in the six-month follow-up. The two groups had a similar total occlusion rate (68.31% and 71.8% respectively), while the complication rate was 3% in group A and 4.7% in group B. Significant differences between the two groups were noted in the number of assisted coiling cases: 28 out of 60 cases (46.7%) in group A - 14 out of 85 cases (16.5%) in group B. Further statistical analysis showed strong dependencies for the type of endovascular procedure between the ruptured and unruptured aneurysms in both groups ($p < 0.000$), but no dependencies between the aneurysm occlusion rate and the ruptured or non-ruptured aneurysms, or between the occlusion rate and the type of endovascular procedure ($p > 0.552$ and 0.071 respectively). In conclusion, the anatomic relation of the aneurysm sac with the wall of the parent artery is important, as significant differences in endovascular practice, devices and techniques were noted between side-wall and bifurcation aneurysms.*

Introduction

The introduction of embolization of cerebral aneurysms using detachable platinum coils by the endovascular route at the beginning of the 1990s^{1,2} revolutionized the management of intracranial aneurysms and subarachnoid hemorrhage. The obvious advantages of aneurysm coiling compared with traditional aneurysm clipping – a method used effectively by the neurosurgical community in aneurysm treatment for years – were also statistically proved with the publication of the International Subarach-

noid Aneurysm Trial (ISAT) in 2002^{3,4}. Since then, embolization – whenever available – has become the treatment of choice for cerebral aneurysms either ruptured⁵ or not⁶. Furthermore, the evolution of new endovascular devices, techniques and materials during the last ten years has given endovascular therapists the ability to treat increasingly difficult, complex-shaped and wide-based aneurysms, enhancing the safety, efficacy and feasibility of endovascular treatment even in cases previously characterized as “untreatable by endovascular means”⁵. This paper describes our experience in the last two years

using a variety of devices and techniques in the endovascular treatment of brain aneurysms. As we have noted differences in the appropriate devices and techniques we need in relation to the anatomic configuration of the aneurysm sac and the parent artery, we decided to attempt a statistical proof of these differences in our practice. For this purpose, we prospectively divided the aneurysms treated during this period into two different groups regarding their relation to the parent artery wall: side-wall (group A) and bifurcation (group B) aneurysms. The goal of this prospective comparison was to identify any statistically significant similarities or differences in endovascular treatment strategy, results and complications between these two groups and to draw any conclusion that will influence or modify our endovascular practice in the future. For this reason, a statistical analysis of the results of our study was planned using the SPSS PASW statistics 18 software.

Patients and Methods

We used a specific protocol organized and dictated by a scientific committee of the National and Kapodistrian University of Athens to record prospectively all patients with saccular intracranial aneurysms treated with coiling during a two-year period (2008-2010). This record included 145 patients with at least one cerebral aneurysm treated by embolization. Eight of these patients had more than one aneurysm, which had been treated in another session and are not included in our study. This prospectively studied population included 94 females and 51 males with an age range between 17 and 84 years and a mean age of 56 years. More than three quarters of the patients (107 aneurysms-73.8%)

presented following rupture and subsequent subarachnoid hemorrhage, while the remainder (38 aneurysms-26.2%) had aneurysms coincidental to the ruptured ones and presented due to mass effect or thromboembolic event or incidental findings during a radiological investigation for some other reason. All the above aneurysms were treated endovascularly by the same endovascular neurosurgeon (AM) using detachable platinum coils. The decision for coiling or clipping was tailored to each single case, taking into account the clinical and neurological situation of the patient as well as the angiographic characteristics of the aneurysm and its relation to the parent artery. As the endovascular neurosurgeon (AM) at our center performs both endovascular *and* neurosurgical procedures with equal results, his decision is based on his unique experience in both fields without being biased by professional issues. Follow-up included clinical evaluation after one, three and six months following the procedure and a cerebral angiogram performed in the six-month period for radiological investigation as well. The immediate angiographic and clinical results as well as the follow-up, including the six-month angiograms, were judged by two independent physicians: a neurosurgeon and an interventional radiologist.

The prospective protocol of our study included division of these aneurysms into two main groups according to their anatomic location among the cerebral arteries (Table 1):

Group A: side-wall (SW) aneurysms

This group included all aneurysms arising either from the supraclinoid internal carotid artery up to its bifurcation, i.e. at the origin of ophthalmic, superior hypophyseal, posterior communicating, anterior choroidal arteries, or from the vertebral or basilar artery trunk, i.e.

Table 1 Total series results (145 endovascularly treated cerebral aneurysms).

Sex	Mean Age	Ruptured	Non-ruptured	Simple coiling	Assisted coiling	Complete occlusion	Complication rate
F 94 M 51	56 yrs	107 (73.8%)	38 (26.2%)	99 (68.4%)	46 (31.6%)	102 (70%)	6 (4.1%)

Table 2 Results in the group A (60 side-wall aneurysms) and group B (85 bifurcation aneurysms).

	Ruptured	Non-ruptured	Simple coiling	Balloon-assisted coiling	Stent-assisted coiling	Total occlusion	Subtotal occlusion	Complications
Group A	38 (63.3%)	22 (36.7%)	32 (53.3%)	15 (25%)	13 (21.7%)	41 (68.3%)	19 (31.7%)	2 (3%)
Group B	69 (81.2%)	16 (18.8%)	71 (83.5%)	12 (14.1%)	2 (2.4%)	61 (71.8%)	24 (28.2)	4 (4.7%)

Figure 1 Side-wall aneurysm before (A) and after (B) coiling.

Figure 2 Bifurcation aneurysm before (A) and after (B) coiling.

at the origin of the posterior inferior cerebellar (PICA), anterior inferior cerebellar (AICA), superior cerebellar (SCA) arteries (Figure 1). Sixty aneurysms of this group were identified among our series: 38 of them (63.3%) were ruptured while 22 (36.7%) were unruptured (Table 2).

Group B: bifurcation (BF) aneurysms

This group included all aneurysms arising from anterior communicating artery (Acom), middle cerebral artery (MCA), anterior cerebral artery distal to the Acom, internal carotid ar-

tery termination and basilar artery termination (Figure 2). This group in our series included 85 aneurysms. Sixty-nine of these treated aneurysms (81.2%) were ruptured while 16 (18.8%) were unruptured (Table 2).

Although this categorization has mainly been used in experimental models⁷⁻⁹ and not very often clinically, we found it extremely interesting from an anatomical and hemodynamic perspective. Many authors have noticed and described the distinct hemodynamic characteristics between BF and SW experimental aneu-

Figure 3 Paraophthalmic aneurysm before (A), immediately after (B) and 6 months after (C) stent and coiling. The stent was used to “jail” a coil tail, which remained in the parent artery. The 6-month angiogram (C) shows the coil tail “outside” the artery (arrow) due to a total reconstruction of the parent artery by stent epithelialization!

rysm models, which play an important role in their formation, shape, growth and rupture^{8,10-13}. Some of them have also reported the important role of these hemodynamic features in clinical aneurysm practice¹⁴⁻¹⁶. The hypothesis that this anatomic relation of the aneurysm sac with its parent artery wall may dictate different methods, devices and techniques of endovascular treatment was the main issue we tried to test in this study. The different characteristics resulting from the comparison between these two groups in our study were statistically tested and analyzed with the use of SPSS PASW statistics 18 software to identify any possible relationships between them. The statistical procedures of Cross tabulations and Chi-square tests (χ^2) were performed for both groups to show any dependencies. Crosstabs is an analysis method of creating a contingency table from the multivariate frequency distributions of two categorical variables.

Results

The total series results, including presentation (ruptured or not), endovascular-assisted devices used as well as occlusion and complication rates are presented in Table 1. These results are similar to most of the published clinical series¹⁷⁻¹⁹. However, the most important issues of this study resulted from the analysis of the results of the two particular groups according to our prospective protocol: groups A and B. In our series, group A with SW aneurysms included 60 cases treated with embolization (Table 2). Thirty-eight of them (63%) presented with subarachnoid hemorrhage following aneurysm rupture while 22 (37%) aneurysms were unruptured. An additional device was used during the coiling procedure in 28 cases (47%): 15 aneurysms were coiled with the balloon-remodeling technique using a temporary compliant balloon (Hyperform – Hyperglide,

ev3) across the aneurysm neck to assist coiling and 13 aneurysms were treated endovascularly with the permanent placement of an intracranial stent at the parent artery deployed before or sometimes after the coiling procedure (Figures 3 and 4). Aneurysm sac occlusion, as judged in the post-embolization angiogram, was characterized as complete or total in 41 aneurysms (68.3%), while it was deemed subtotal in 19 aneurysms (31.7%). Seven of these subtotally occluded aneurysms were unruptured while 12 of them were ruptured. Complications related to the embolization procedure (angiographic only and/or clinical) were noted in five cases including three thromboembolic events and two intraprocedural ruptures. However, most of them (three out of five) were temporary, with the patient making a complete clinical and neurological recovery within a week after the procedure. A permanent neurologic deficit remained in two cases (3%) although it improved during the follow-up period (up to six months after the procedure). No angiographic recurrence was noted in any of the aneurysms in this group at the six-month angiographic follow-up, and these results were stable even in the subtotally occluded lesions. Remarkably, further and more stable occlusion was noted in two thirds of them (13 out of 19) in relation to the initial post-embolization angiogram (Table 3). This phenomenon was even more remarkable in cases where a stent had been also deployed to assist coiling: epithelialization of the stent inner surface among the parent artery endothelium was noted in all these cases, improving and stabilizing the aneurysm sac occlusion but also improving the parent artery inner surface, sometimes even organizing and producing a new parent artery flow diversion (Figure 3).

Figure 4 Conventional and assisted coiling in group A (60 side-wall aneurysms) and group B (85 bifurcation aneurysms).

Group B comprised 85 BF aneurysms (Table 2). Sixty-nine of them (81%) were ruptured aneurysms while only 16 (19%) were unruptured. In the vast majority (71 aneurysms – 83.5%), endovascular treatment included coiling using detachable platinum coils without any additional devices and only 14 of them (16.5%) underwent a balloon-remodeling technique (12 aneurysms) or stent-assisted coiling (two aneurysms) (Figure 4). Aneurysm sac occlusion, according to the post-embolization angiogram judgment, was complete in 61 aneurysms (71.8%), while it was deemed subtotal in 24 of them (28.2%). Eighteen of the subtotally occluded aneurysms were ruptured while six were unruptured. Complications related to the embolization procedure (angiographic only and/or clinical) were noted in 13 cases: eight of them were thromboembolic while five were related to aneurysm rupture during the coiling procedure. However, the majority of complications had either no (four out of 13) or only tem-

Table 3 Six-month angiographic follow-up results in group A (60 side-wall aneurysms) and group B (85 bifurcation aneurysms). No angiographic recurrence was noted in any of the treated aneurysms in this series. The totally occluded aneurysms were found stable at the 6-month follow-up. Among the subtotally occluded aneurysms, 68.42% of group A and 62.5% of group B showed further angiographic occlusion at the 6-month control; 31.58% and 37.5% respectively remain unchanged.

	<i>Ruptured</i>	<i>Non-ruptured</i>	<i>Totally occluded aneurysms</i>	<i>Changes among total occluded aneurysms after 6 months</i>	<i>Subtotally occluded aneurysms</i>	<i>Further occlusion after 6 months</i>	<i>Unchanged after 6 months</i>	<i>Recurrence after 6 months</i>
Group A	38 (63.3%)	22 (36.7%)	41 (68.3%)	0 (stable occlusion in all 41 aneurysms)	19 (31.7%)	13 (68.42%)	6 (31.58%)	0
Group B	69 (81%)	16 (19%)	61 (71.8%)	0 (stable occlusion in all 61 aneurysms)	24 (28.2%)	15 (62.5%)	9 (37.5%)	0

porary (five out of 13) clinical sequelae, with permanent neurologic deficit in only four patients (two due to ischemic infarct and two due to re-rupture) and a morbidity rate of 4.7%. The late angiographic result in the six-month angiographic follow-up was stable or improved (Table 3) in all cases and no recurrence was noted among the aneurysms of this group either. The aneurysms found totally occluded in the six-month angiogram were discharged from further follow-up as this result is assumed to be a cure. For the subtotal occluded aneurysms, further follow-up is necessary and this is planned using magnetic resonance angiography. If aneurysm recanalization is found in the future follow-up, a new endovascular procedure may be necessary, but such a decision should be made on an individual basis taking into account the related clinical parameters as well as radiological features.

Statistical analysis of the results of our series showed that there is a strong dependency between the type of endovascular procedure (simple coiling or assisted coiling using a balloon or a stent) and between the ruptured and unruptured aneurysms in both groups (p -value for Pearson's Chi-square was very low, $0.000 < 0.05$). On the other hand, no dependencies were noted between the occlusion aneurysm rate and the ruptured or non-ruptured aneurysms, or between the occlusion rate and the type of endovascular procedure (simple coiling, balloon-remodeling or stent), as the p -values for Pearson's Chi-square were very high ($0.552 > 0.05$ and $0.071 > 0.05$ respectively).

Discussion

Endovascular treatment of cerebral aneurysms using detachable platinum coils has evolved dramatically since its introduction in 1991^{1,2} and is currently the first choice treatment for brain aneurysms worldwide^{5,6}. In our Department, the Chief of the Neurovascular Service (AM) is a neurosurgeon with special training in endovascular neurosurgery so that the decision on the type of procedure (open surgical or endovascular) is made in an individual basis. However, during the last five years, the vast majority of aneurysms (more than 90% of ruptured and almost 80% of unruptured) have been treated by endovascular means, leaving only the remainder for clipping in a craniotomy procedure. The tremendous advances in endovascular techniques, devices and materials

have played a significant role towards this direction by extending the ability of catheter-based techniques to treat more and more cerebrovascular diseases related to brain aneurysms²⁰.

The balloon-remodeling technique using new compliant balloons designed exclusively for intracranial use, was the most important technical improvement in brain aneurysm embolization after the introduction of detachable platinum coils. This technique made us able to treat more complex and wide-necked aneurysms previously deemed untreatable by endovascular means, making the method safer and more efficient²¹⁻²⁷. The latest generation coils with a huge selection of size, shape and deployment behaviour and with different bioactive characteristics have significantly widened the armamentarium of endovascular therapists^{28,29}. The introduction of a variety of new stents exclusively designed for the intracranial arteries is also another important advance in the endovascular therapy of cerebrovascular lesions. The combination of coiling support as well as flow diversion and reconstruction of the parent artery endothelium (Figure 3) obviously offers further advantages but the long-term results need to be evaluated³⁰⁻³⁷. New endovascular devices (resulting from stent technology and experience), currently called flow-diverters (Pipeline flow-diverter, ev3, FDA approved June 8, 2011), have started to be implanted endovascularly across the neck of wide-based large or giant aneurysms in an attempt to occlude the aneurysm sac without coils maintaining the patency of the parent artery lumen. The first results of the use of flow diverters are encouraging³⁸ and these devices may be the next revolutionary step in endovascular aneurysm therapy.

In relation to all the above developments, it has now become mandatory for the neuroendovascular therapist to use this array of new devices and techniques in the most appropriate way³⁹. Although in most circumstances, each aneurysm responds uniquely to embolic devices, there are common characteristics which can help in the selection of the optimal therapeutic modality. An attempt in this direction was the main aim of this study analyzing and evaluating the aneurysms treated in a single center by one endovascular surgeon during a two-year period following a specific prospective protocol dictated by a scientific committee of Athens University. Interesting findings in this study stemmed from the prospective characterization of the treated aneurysms in the two anatomical groups according to the above prospective protocol: side-

wall (SW) and bifurcation (BF) aneurysms. This characterization has mainly been adopted in experimental aneurysm studies in animal⁷⁻¹⁰, artificial silicone^{11,12} or more recently in computer fluid dynamic models⁴⁰⁻⁴³. Although aneurysms of the same group may be located in different parent arteries in the circle of Willis (i.e. a Pcom and an SCA aneurysm), they may share many common anatomic and hemodynamic features which could strongly influence their formation, growth, clinical presentation and appropriate embolization techniques and results.

It is common knowledge that the most frequent clinical presentation of an intracranial aneurysm is subarachnoid hemorrhage due to its rupture, resulting in significantly high morbidity and mortality^{44,45} and this was also the rule in our series. However, the ratio between ruptured and unruptured aneurysms differed in the two groups of our study. Although the majority of aneurysms were ruptured in both groups, in BF aneurysms the ratio was 4:1 whereas in SW aneurysms the ratio was only 3:2 in favor of the ruptured lesions respectively. This statistically significant variation between the two groups is probably due to hemodynamic and anatomical reasons. Aneurysms created on major branching points of cerebral arteries usually rupture at a smaller size for hemodynamic reasons, while side-wall aneurysms suffer less directly from the hemodynamic shear stress and may exist for a longer period of time before their sac reaches a larger size and ruptures. This hypothesis is further supported by the fact that the vast majority of large and giant aneurysms belong to the SW type and they are often identified before they rupture, usually presenting with mass effect (i.e. a Pcom aneurysm with third nerve palsy or a vertebral aneurysm with lower brainstem signs and symptoms) or thromboembolic events.

Reviewing the literature, there are two different strategies for assistance during coiling: either use in advance some kind of assistance in almost all cases²⁶ or use in selected cases where specific indications exist²⁵. We adopted the second strategy using a balloon or stent to support coiling only when we judged it appropriate. Following this strategy however, we noted remarkable variations regarding coiling assistance between the two different groups of our series (Figure 4). In the SW group, assistance was used in a significant number of cases (47%): in almost half (15 cases) of them the device used was a temporary balloon while in the remainder¹³ it was an intracranial stent. At the same

time, the assisted coiling in the BF group was used in significantly fewer cases: only 14 of the 85 treated aneurysms (16.5%), using a balloon in the vast majority (12 cases) and a stent only in two of them. The reasons for this statistically significant variation between the two groups can also be found in clinical and anatomic features. As already mentioned, the number of ruptured aneurysms in the BF group was significantly higher, with more patients presenting immediately after subarachnoid hemorrhage. Thus, we did not have the opportunity to prepare them appropriately with antiplatelet medication according to the stent protocol and the use of a stent was excluded in most of these cases. This fact gives a reliable explanation for the limitations in stent use. However, stent use was also less frequent with the balloon-assisted technique in the BF group. The main clinical factor responsible for this is the higher number of unruptured, "cold" cases in the SW group. These endovascular procedures are designed and performed in a scheduled manner, without the stress of an urgent subarachnoid event. The majority of these patients are in a stable – frequently normal – physical and neurological condition and not in a critical condition as after a subarachnoid hemorrhage with an angry and swollen brain and the patient having moderate or major neurologic deficits. Furthermore, anatomical reasons in aneurysms of the SW group such as larger size, wider neck, less favorable neck-to-sac ratio, more proximal aneurysm location in the circle of Willis, higher demands for better microcatheter stabilization inside the aneurysm sac and the need for better packing results and flow diversion to lessen the likelihood of recurrence lead us to more frequent use of the assisted coiling techniques and devices among the aneurysms of this group.

There is common agreement that by using the above techniques we are able to enhance the safety and efficacy of endovascular aneurysm treatment. However, to our surprise the use of these devices did not alter the occlusion rate in our series, as the immediate complete occlusion rate was 71.8% in the BF group and 68.3% in the SW group, a not statistically significant difference presenting similar results between the two groups. Nor did these results change in the six-month angiographic follow-up. Although these findings in our series look peculiar, by practical means, we *did* have better results in the *selected* cases in which we used a balloon or a stent following our criteria, as most of these cases were large, wide-necked and complex an-

eurysms, most of which may be untreatable without the application of these techniques.

Regarding the complication rate, the comparison between the two groups revealed a lower rate in the SW group, although more cases in this group underwent assisted coiling. This is in agreement with most of the published literature on assisted coiling series⁴⁶. Although there were some concerns regarding the possibilities of higher complication rates due to thromboembolic events using balloon-remodeling techniques²³, most authors have reported no differences in the complication rate using these techniques either with the new-generation compliant balloons²⁴⁻²⁷ or with one of the newly exclusively designed intracranial stents³³⁻³⁷. Albayram et al.⁴⁶ compared the incidence of thromboembolic events with balloon-assisted and conventional coiling using diffusion-weighted (DW) imaging within six hours following the procedure, reporting no significant differences between the two groups. Furthermore, Brooks et al.⁴⁷, using similar DW imaging techniques, reported that the use of adjunctive coiling techniques such as balloons or stents did not appear to increase the frequency of embolic or ischemic events. Regarding the subtotally occluded aneurysm group, further follow-up is definitely necessary. However, the relatively high number of these is related to angiographic characteristics and they do not present a real risk to the patient. Future treatment decisions should be based on both the angiographic evolution of these aneurysms in relation to their clinical parameters on an individual basis. Reports of larger series in

the literature have shown that only a minority of them will need an additional procedure in the future⁴⁸.

The main limitations of our study are due to the relatively small number of cases included and the fact that these cases come from one center and were treated by one neuroendovascular surgeon. However, these characteristics may be beneficial as they have created a very "compact" uniform group of patients not biased by variations in population characteristics, personal treatment preferences and experience or limitations in the available endovascular devices (older versus newer better designed devices), making our conclusions quite reliable.

In conclusion, our prospective study has shown that BF aneurysms may be more prone to rupture and at a smaller size than SW lesions. This conclusion may influence our decision on how to treat an unruptured aneurysm if the lesion has the anatomic characteristics of a BF type lesion. On the other hand, the use of assisted coiling is more frequently necessary in SW aneurysms, and does not raise the complication rate or add further risk to the endovascular treatment. These remarks maybe useful for the endovascular therapist and should be taken into account when planning endovascular strategy and may help us to be better prepared and use all the available devices and techniques in the most appropriate way. Larger series comparing SW and BF aneurysms are definitely necessary for even safer and more reliable findings and conclusions to assist and successfully direct our daily clinical and endovascular practice.

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