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Title Page

Endovascular treatment of distal anterior cerebral artery aneurysms: long-term results

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Abbreviations: **DACA** = distal anterior cerebral artery; **SAH** = subarachnoid hemorrhage; **IPH** = intraparenchymal hematoma; **GOS** = Glasgow Outcome Scale; **HH** = Hunt and Hess Scale

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Endovascular treatment of distal anterior cerebral artery aneurysms: long-term results

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Abstract

Background and Purpose. Endovascular therapy is the first-line therapeutic option for intracranial aneurysms, however the results of the endovascular approach for distal anterior cerebral artery (DACA) aneurysms are not well known. We assessed the immediate and long-term clinical and angiographic outcomes after endovascular coiling of DACA aneurysms.

Materials and Methods. We performed a retrospective analysis of all consecutive DACA aneurysms treated by endovascular coiling. Procedural complications, clinical, and angiographic results were prospectively recorded in an institutional aneurysm database between 1992 and 2013.

Results. Satisfactory initial occlusion was achieved for 85.9% of cases (79/92). There were three cases of intraprocedural rupture of the aneurysmal sac and three treatment failures, all involving small aneurysms (<4 mm). Rates of procedure-related mortality and morbidity were respectively 1.1% and 0%. Scores of 5 (good recovery) or 4 (moderate disability) on the Glasgow Outcome Scale, indicating favorable outcome, were observed for 79.3% of patients (73/92) at hospital discharge. In follow-up, 13 cases of recanalization were observed, 12 of which were classified as major. Ten of the recanalizations underwent a complementary intervention.

Conclusion. The endovascular management of DACA aneurysms appears to be efficacious and safe, although certain technical difficulties may emerge when aneurysms are small. A higher proportion of major recanalization events may imply a more frequent deployment of complementary interventions in comparison to aneurysms situated elsewhere.

Introduction

Distal anterior cerebral artery (DACA) aneurysms, comprised between the segments A2 to A5 of the anterior cerebral artery (i.e. the pericallosal artery), represent 2 to 9% of intracranial aneurysms.⁽¹⁻³⁾ They are notable for their frequent association with other aneurysms,⁽²⁻⁶⁾ a high incidence of rupture at diagnosis,^(2,6) the association of both subarachnoid hemorrhage (SAH) and intraparenchymal hematoma (IPH) for ruptured aneurysms,^(4,7,8) and high morbidity and mortality rates after treatment.⁽¹⁾ The surgical clipping of DACA aneurysms by the inter-hemispheric approach presents some technical challenges due to a restrained operative field, difficulties in controlling the parent artery, and often unfavorable orientation of the aneurysmal sac and adhesions at the cingulate gyri.⁽⁹⁾ A high morbidity rate, ranging from 12% to 25%, were reported.^(5,6) Endovascular treatment also has the reputation of being challenging. Some authors reported higher frequencies of procedural sac perforation for DACA aneurysms than for others, and higher frequencies of coiling failure due to their small size and distal location.⁽¹⁰⁻¹²⁾ The aim of this study was to retrospectively assess the clinical and anatomical results after endovascular coiling of DACA aneurysms in the long term.

Patients and Methods

Study Population and Data Collection

Since October 1992, date at which we began using detachable coils in our department, all patients for whom an endovascular treatment is indicated are included prospectively in a dedicated registry. Recorded information includes patient clinical data (personal and family history, Hunt and Hess (HH) and World Federation of Neurosurgical Societies (WFNS) scales at admission), delay to treatment, aneurysm characteristics, and clinical and

angiographic results, both immediate and in follow-up. A retrospective analysis of our DACA aneurysms treated by endovascular approach was performed.

Endovascular Treatment

Endovascular treatment was performed under general anesthesia on a biplane angi suite. In 1997, 3D angiography (Butterfly System then Innova flat-panel detector, GE Healthcare, Chicago, Illinois) was added to the protocol. All endovascular interventions were done under full anticoagulation with heparin (loading dose of 2000 to 3000 IU followed by continuous infusion of 20 to 40 IU/kg/hour), and postprocedural treatment included a one-month antiplatelet therapy (a daily dose of 75 mg of aspirin for unruptured aneurysms or a daily dose of 100 mg of flurbiprofen for the ruptured ones). Additionally, in patients who had recent subarachnoid hemorrhage (<30 days), nimodipine (2 mg/hour) was administered intravenously for the totality of the intervention and continued postprocedurally for 14 to 21 days.

Endovascular treatment consisted in a placement of a 6F guiding catheter as distally as possible in the cervical portion of the internal carotid artery, followed by a selective catheterization to the aneurysm and the filling of this latter with simple platinum coils as compactly as possible without remodeling. The main microcatheters used were the Excel 10 microcatheter and the Turbo Tracker 18 (Target Therapeutics, Fremont, California) up till the mid-2000s, then the Echelon 10 or 14 microcatheters (eV3 Neurovascular, Irvine, California) were used predominantly thereafter. Only uncoated Guglielmi detachable coils were used during the study period (bioactive coils such as polyglycolic/poly-lactic acid-coated coils or hydrogel-coated coils were not applied in this series).

No adjunctive techniques such as balloon-assisted coiling or stents were used, because of the small caliber of the DACA and the distal location of aneurysms.

Clinical and Angiographic Follow-Up

The patients were monitored by the interventional neuroradiologist during their hospitalization and evaluated at discharge with the Glasgow Outcome Scale (GOS), graded from 1 (death) to 5 (good recovery). Thereafter, they were received for follow-up visits at 6 weeks, 6 months, and 1, 3 and 5 years after treatment and reevaluated with the GOS. The patients underwent 3D time-of-flight (TOF) magnetic resonance angiography and/or digital subtraction angiography at 6 months, and thereafter at 1, 3, and 5 years. All patients received for follow-up had at least one angiographic evaluation at one year.

The degree of aneurysm occlusion was classified by using the simplified 3-point scale: total for complete occlusion of the sac and neck; subtotal when a residue persisted at the neck; and partial when there was residual opacification within the aneurysmal sac (complete occlusion, neck remnant, aneurysm remnant).⁽¹³⁾ Total and subtotal occlusions were considered satisfactory. In follow-up, recanalizations were considered minor when occlusion went from total to subtotal, or major when occlusion became partial.

Statistical Analysis

Qualitative variables were compared with the Fisher's exact test or the Pearson's chi-squared test. Quantitative variables were compared with the Student's t-test. Statistical significance was set at $P \leq 0.05$.

Ethical statement

In accordance with the French legislation, Institutional or Ethics Committee approval was not required for this study because it only utilized anonymized data collected as part of routine clinical care.

Results

Between October 1992 and October 2013, 2297 patients with 2738 aneurysms were included in our database. A total of 92 DACA aneurysms (73 ruptured, 19 unruptured) were treated during the study period. Patients with DACA aneurysms were aged 27 to 86 years with a mean age of 54 years, and were predominately female (61 women; 66.3%).

Baseline Aneurysm Characteristics

The mean size of DACA aneurysms was 4.9 ± 3.1 mm (**Table 1**). The aneurysms were classified by size along their longest axes into four groups: small <4 mm (31; 33.7%), medium from 4 to 10 mm (50; 54.3%), large from >10 to 20 mm (10; 10.9%) and giant >20 mm (1; 1.1%). A small neck (neck size/aneurysm sac size ratio $\leq 1/2$) was observed in 32 aneurysms (34.8%), medium neck ($1/2 < \text{ratio} \leq 1$) in 56 (60.9%), and wide neck (ratio >1) in 4 aneurysms (4.3%).

Seventy-three (79.3%) of the DACA aneurysms were ruptured at diagnosis, and subarachnoid hemorrhage was associated with an IPH in the frontal lobe, corpus callosum or cingulate gyrus in 40 patients (54.8%), and with intraventricular hemorrhage in 53 patients (72.6%).

Procedural Complications

Complications occurred during seven of the endovascular interventions (7.6%).

Three perforations (3.3%) were noted during aneurysm coiling. Two of them were treated by coiling with satisfactory results. The third was converted to uneventful surgical clipping. All three of these cases involved small aneurysms measuring less than 4 mm.

Three thrombo-embolic events (3.3%) were observed. All three were resolved successfully without radioanatomic complication or postoperative clinical deficit, via the intravenous administration of abciximab (GpIIb-IIIa inhibitor) in a 0.25 mg/kg bolus followed by a 0.125

µg/kg/min continuous infusion for 12 hours. One of the cases was a ruptured aneurysm with a Fisher grade 4 SAH without associated IPH; there was no aggravation of bleeding.

The remaining intraprocedural complication (1.1%) involved an aneurysm located at the bifurcation of the callosal-marginal artery: a coil movement created a protrusion in the lumen of that artery. Although the aneurysm itself was subtotally occluded, the obstruction in the callosal-marginal lumen could not be resolved satisfactorily, resulting in extensive frontal lobe ischemia with severe motor and cognitive deficits. The patient, who suffered from serious cardiovascular comorbidities, died from severe pneumonia one month later.

Initial Anatomical Results

Endovascular treatment failure was observed for three DACA aneurysms (3.3%). Two of the failures were related to vasospasms and one to coil instability. All three of these cases involved small aneurysms (<4 mm).

However, the ratios of neck width to sac diameter of the three aneurysms were all different and thus unsuggestive of a role for aneurysmal neck width in endovascular treatment failure.

Initial occlusion was satisfactory for 79 aneurysms (85.9%), with a total occlusion for 22 (23.9%), and subtotal for 57 (62%) aneurysms. Partial occlusion was observed for 10 aneurysms (10.9%) and treatment failed for the remaining 3 aneurysms (3.3%). Patients with ruptured aneurysms who presented an IPH at admission had a significantly lower rate of total occlusion (5 of 40 patients, 12.5%) than those who did not (11 of 33 patients, 33.3%; $P=0.046$). No difference was observed in terms of satisfactory occlusion (87.5% vs 87.9%) (**Table 2**).

Postoperative Clinical Outcome

At discharge, 73 of the 92 patients (79.3%) had satisfactory outcomes, with GOS scores of 5 for 61 (66.3%), and 4 for 12 (13%). Sixteen patients (17.4%) had unfavorable GOS scores (3 or 2) and three patients died before discharge (see below).

Among the 19 patients with unruptured aneurysms (HH 0 group), 18 were GOS 5 (94.7%) and one was GOS 4 (5.3%), and among the 73 patients with ruptured aneurysms, 43 were GOS 5 (58.9%) and 11 GOS 4 (15.1%).

Outcomes varied as a function of HH score at hospital admission. The 44 patients with HH scores of 1 or 2 had clinical outcomes at discharge similar to patients with unruptured aneurysms: 43 were GOS 5 (97.7%) and one was GOS 4 (2.3%). In contrast, of the 12 patients with HH scores of 4 or 5, only two (16.7%) left the hospital with a satisfactory clinical condition (GOS 4) (**Table 3**).

Three patients, all with ruptured aneurysms, died during the initial hospitalization. The first died from a rebleeding event before the endovascular intervention and the second from acute cardiac decompensation. The third patient died from an intraoperative coil displacement and resulting ischemia described above. Thus, the procedure-related mortality rate was 1.1%.

Long-Term Clinical Outcomes

Mean follow-up was 4.5 ± 1.3 years. Outcomes in follow-up were favorable (GOS 5 and 4) for 75 of 92 patients (81.5%) at six weeks, 80 of 88 (90.9%) at six months, 81 of 88 (92%) at one year, 73 of 78 (93.6%) at three years, and 70 of 75 (93.3%) at five years.

Two deaths occurred during the follow-up period, one at four months and the other at three years after the initial intervention. Both patients had ruptured aneurysms but neither of the deaths were due to neurological causes. There were no bleeding incidents in the follow-up period.

The presence of SAH and IPH was significantly associated with poorer outcome at five years: A GOS score of 5 at five years was observed in only 42.5% of patients with IPH (17/40) compared to 87.9% of patients without IPH (29/33), $p < 0.001$.

Long-Term Anatomical Outcomes

Occlusion was satisfactory for 73 of 88 aneurysms at six months (83%), for 63 of 88 at one year (71.6%), for 53 of 78 at three years (67.9%), and for 50 of 75 at five years (66.7%). Recanalization occurred in 13 of the 75 aneurysms treated and monitored out to five years, i.e., a global recanalization rate of 17.3%. One recanalization case was considered minor and the twelve others major (**Figure**). Twelve recanalizations appeared within the first year of follow-up and one between three and five years.

A complementary intervention was performed for 10 of the major recanalization cases, and these interventions were surgical for two cases and endovascular for eight. Among these latter cases, total occlusion was achieved for two and subtotal occlusion for six of them, all remaining stable thereafter. The three other cases of recanalization (2 major, 1 minor), were assigned to surveillance due to a complex morphology of the aneurysm remnant, without rupture.

Occlusion evolution depended significantly on initial occlusion ($p = 0.044$). Among the 21 aneurysms occluded totally in the initial intervention and monitored for the full five years, there was only one case of major recanalization (4.8%), which occurred at three years. Thus, 95.2% of total occlusions remained stable. In contrast, among the 41 initially subtotal occlusions with five years of follow-up, there were 12 cases of recanalization (29.3%), 11 major and one minor, most (11) occurring within the first year. Thus, only 70.7% of subtotal occlusions remained stable.

Discussion

Our endovascular series relating to the endovascular treatment of DACA aneurysms is one of the largest published to date, and one of the few with a long-term follow-up. In our prospective single center cohort, endovascular therapy of DACA aneurysms appeared to be efficient and safe.

Intraprocedural rupture is a common complication of DACA aneurysms. The literature reports rates for it ranging from 7% to 16%,^(6,7,10,11,14) but in our series it was only 3.3%. Our intraprocedural rupture rate was also lower than that estimated for all-locations small (<3 mm) aneurysms, i.e., from 7% to 8%.^(15,16)

The literature reports rates for procedure-related mortality ranging from 2.6% to 9%, and for procedure-related morbidity of approximately 8%.^(6,7,8,11,14) The rates for these aspects in our series were lower, respectively 1.1% and 0%.

With frequencies varying from 3.3% in our series to 10% in that of Yamazaki et al.,⁽¹⁷⁾ endovascular treatment failure is most commonly associated with difficulties encountered in the catheterization of distal arteries or the stabilization of coils in a small aneurysmal sac.^(6,17)

The immediate anatomical results of our endovascular interventions were satisfactory (total or subtotal occlusion) in 85.9% of cases (78.9% for unruptured (15/19), and 87.7% for ruptured (64/73) aneurysms). These rates were comparable with those previously reported in the literature.^(4,14,17,18)

Several studies have shown that outcomes of DACA aneurysms depend on the neurological status of the patient at admission,^(4,8,14) and our study did so as well. Indeed, considering our patients who presented with rupture aneurysms, 43 of the 44 (97.7%) patients who had favorable HH scores of 1 or 2 at admission had GOS scores of 5 at discharge, whereas only

10 of the 29 patients (34.5%) who had unfavorable HH scores ≥ 3 had GOS scores of 4 at discharge, and none had GOS scores of 5.

The mean rebleeding rate for ruptured aneurysms in general is 3.2% but that for DACA aneurysms is usually reported to be higher, at about 7%.⁽¹⁸⁾ This however was not observed in our study, where the rebleeding rate after treatment was 0%.

Our recanalization rate of 17.3% was coherent with other recently-reported series,^(11,14,19) but not higher than all-locations recanalization rates, ranging from 20% to 33% for intracranial aneurysms.^(3,20) However, we did see a very high proportion of major recanalizations (12 of 13 cases; 92.3%). In two other recently-reported series,^(21,22) much lower rates of major recanalizations were reported, i.e., 16% and 25%, but we note that the populations of those studies, respectively 16 and 23 patients, were smaller than ours (92 patients).

A second intervention was performed for 77% (10/13) of our recanalization cases, a rate much higher than that observed for intracranial aneurysms in general (estimated between 35% and 49%),^(3,23,24) but logically explained by our high proportion of major recanalization cases necessitating additional care.

It is generally accepted that the quality of the initial occlusion of an intracranial aneurysm conditions its evolution thereafter.^(3,23,25-27) This appeared to hold true for the DACA aneurysms in our series: recanalization occurred in 29.3% of the aneurysms initially occluded subtotally, but in only 4.8% of those occluded totally.

Ruptured DACA aneurysms are often associated with IPH at diagnosis.^(4,6,8,17,18) The rate of IPH in our ruptured aneurysms was 54.8%, which falls within the range of rates of 41% to 63% reported in recent studies.^(4,8,17,18) The frequency of IPH in ruptured DACA aneurysms may be explained by the low volume of the pericallosal cistern and the close contact between the aneurysm and the adjacent cerebral parenchyma.

In our work, the presence of an IPH influenced initial occlusion: total occlusion was achieved for 33.3% of ruptured aneurysms without IPH vs 12.5% of those with it. This influence was also demonstrated by Oishi et al. in 2013.⁽¹⁸⁾

IPH presence at diagnosis also plays a role in clinical outcomes over time. In coherence with the present literature,^(7,8) we observed a GOS score of 5 at five years for 87.9% of patients without IPH at admission but for only 42.5% of those with it.

We do note several limits to the work presented here, particularly its retrospective design and the number of patients lost to follow-up at five years (12 in all, or 13% of the initial population of 92 patients).

Conclusion

In our prospective single center cohort, endovascular therapy of DACA aneurysms has been efficacious and safe, although associated with certain technical difficulties when aneurysmal sac size is small. Our results suggest that recanalization rate is similar to those reported for other intracranial locations; however, when recanalization occurs, it is frequently major, and may result in a higher rate of complementary interventions.

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Table 1. Baseline characteristics

	Ruptured aneurysms	Unruptured aneurysms
Patient characteristics		
Number	73	19
Sex (number F / M)	48 / 25	13/6
Mean age	55.5 years	52.3 years
Aneurysm sizes (mm)		
Minimum - maximum	2 - 20	2 - 7.4
Mean	5.4	4.4
Standard deviation	3.3	1.8
Median	4.4	4.5

F: female; M: male

Table 2. Initial aneurysm occlusion.

	Ruptured aneurysms		Unruptured aneurysms	Total
	IPH +	IPH -		
Satisfactory	35 (87.5%)	29 (87.9%)	15 (78.9%)	79
Total	5 (12.5%)	11 (33.3%)	6 (31.6%)	22
Subtotal	30 (75%)	18 (54.6%)	9 (47.3%)	57
Partial	4 (10%)	3 (9.1%)	3 (15.8%)	10
Treatment failure	1 (2.5%)	1 (3%)	1 (5.3%)	3
	40	33	19	92

IPH +: presence of an intraparenchymal hematoma at admission.

IPH -: absence of an intraparenchymal hematoma at admission.

Table 3. Clinical outcome at discharge according to the clinical status at admission.

	GOS 5	GOS 4	GOS 3	GOS 2	GOS 1	Total
HH 0	18	1	0	0	0	19
HH 1	18	0	0	0	0	18
HH 2	25	1	0	0	0	26
HH 3	0	8	6	1	2	17
HH 4	0	2	7	0	1	10
HH 5	0	0	1	1	0	2
Total	61	12	14	2	3	92

HH: Hunt and Hess scale at admission; HH 0: unruptured aneurysm

GOS: Glasgow Outcome Scale at hospital discharge

Figure. Recanalization occurred in 13 of the 75 aneurysms treated and monitored out to five years. (A) DSA in working projection shows a ruptured DACA aneurysm arising from the A3 segment in a 55-year-old woman. (B) The patient underwent uneventful coiling. Total occlusion was achieved. (C) DSA in working projection at three years after treatment reveals a major recanalization.

