

# Endovascular therapy for selected (most non-surgical) intracranial aneurysms in a Brazilian University Hospital

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## ABSTRACT

**Objective:** The objective of this study was to evaluate technical, clinical and angiographic results of a nonsurgical series of intracranial aneurysms treated by endovascular approach at Hospital das Clínicas of Medical School of Ribeirão Preto - University of São Paulo.

**Method:** Between August 2005 and November 2008, 137 aneurysms in 106 patients were endovascularly treated. Of these, 101 were unruptured in 75 patients and 36 aneurysms in 31 patients were treated during the acute phase. The data were prospectively studied.

**Results:** Sixty three aneurysms (46%) were treated with coils alone, 52 (38%) with balloon remodeling, 15 (10.9%) with stent remodeling, and 7 (5.1%) with therapeutic occlusion of the internal carotid artery. Six clinical complications (5.7%) were related to the procedures, 3 (2.8%) transitory and 3 (2.8%) permanent. Angiographic follow-up was available for 97 aneurysms (70.8%), clinical monitoring for 77 patients (72.6%) and telephone contact for 97 (91.5%). **Conclusion:** The technical, clinical and angiographic results found in this study are similar to those reported in the literature.

**Key words:** intracranial aneurysm, endovascular treatment, remodeling technique, socioeconomics, complications.

## Tratamento endovascular de aneurismas selecionados (maioria não cirúrgicos) em um hospital universitário brasileiro

## RESUMO

**Objetivo:** Nosso objetivo foi avaliar os resultados técnicos, clínicos e angiográficos de uma série de aneurismas intracranianos não cirúrgicos tratados por via endovascular no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo e comparar com os dados disponíveis na literatura atualmente. **Método:** Entre agosto de 2005 e novembro de 2008, 137 aneurismas foram tratados por via endovascular em 106 pacientes. Destes, 101 eram não rotos em 75 pacientes e 36 aneurismas foram tratados em 31 pacientes durante a fase aguda de ruptura. Os dados foram incluídos de maneira prospectiva. **Resultados:** Sessenta e três aneurismas (46%) foram tratados com técnica simples, 52 (38%) com remodelagem por balão, 15 (10,9%) com remodelagem por stent e 7 (5,1%) por oclusão terapêutica da carótida interna. Seis complicações clínicas ocorreram (5,7%), 3 (2,8%) transitórias e 3 (2,8%) permanentes. Seguimento angiográfico foi realizado para 97 aneurismas (70,8%), clínico para 77 pacientes (70,8%) e contato telefônico para 97 pacientes (91,5%). **Conclusão:** Os resultados encontrados nesta série, em termos técnicos, clínicos e angiográficos, são semelhantes aos encontrados na literatura.

**Palavras-chave:** aneurisma intracraniano, tratamento endovascular, técnica de remodelagem, fatores socioeconômicos, complicações.

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Endovascular treatment of cerebral aneurysms underwent a revolution after the introduction of controlled detachable coils<sup>1</sup>. The first series available in the literature reported the results only for aneurysms not suited for surgery<sup>2,3</sup>. In 2002 the ISAT study<sup>4</sup> demonstrated at level 1 of evidence that ruptured cerebral aneurysms significantly benefited from endovascular treatment, changing the treatment of cerebral aneurysms all over the world. Unfortunately, this achievement may not be reproducible in many developing countries, since there are no many publications showing their results<sup>5</sup> and many factors hinder the development of the technique.

Initially restricted to small neck aneurysms, balloon<sup>6</sup> and stent<sup>7,8</sup> remodeling, allied to therapeutic occlusion of the internal carotid artery (ICA)<sup>9</sup> have allowed the treatment of the majority of intracranial aneurysms.

Our study comprises a population of most non-surgical aneurysms treated by endovascular approach at the Medical School of Ribeirão Preto, University of São Paulo, after the recent establishment of interventional neuroradiology discipline. The patients included in the study were considered unsuitable for surgical approach by the vascular neurosurgeons of the institution. Factors related to complications and treatment stability have been analyzed and compared to the results in the literature.

## METHOD

This prospective study period began with the first patient treated in August 2005 and ended with the last treatment included in November 2008. Collected data included demographic information, aneurysms characteristics, treatment strategy, angiographic results, clinical condition at admission and discharge, clinical follow-up and telephone interview. Retreatments and their results were also included.

This research was approved by the ethical committee of our institution and all the patients had their inclusion in the study authorized by an informed consent.

The patients were divided into two groups to analyze the clinical results: with unruptured and ruptured aneurysms. Technical results and stability were analyzed considering the entire group.

Inclusion criteria were: risky location or inaccessible for surgery; patients with critical clinical conditions; multiple aneurysms, one of which already treated surgically, patients with residual aneurysm after surgery, and patient's option for endovascular treatment.

Aneurysms considered suitable for surgery were excluded by the vascular neurosurgical team, without the participation of the interventional neuroradiology in this decision.

All procedures were performed on a monoplane angiographic system without 3-dimensional reconstruction.

The procedures were performed under general anesthesia (GA) and a 5000UI bolus of heparin was administered followed by 2500-3000UI continuously after the digital subtracted angiography (DSA). In the absence of complications, heparin was ceased at the end of the procedure.

Antiplatelets were not used as routine preparation for the endovascular treatment of ruptured or unruptured aneurysms. However, aneurysms treated with stent remodeling received 300mg aspirin and 75mg clopidogrel per day 5 days before the procedure, continued for 6 months, followed by aspirin alone for 1 year.

After analyzing the aneurysm, one of these 4 therapeutic alternatives was chosen: [1] coils alone for small neck aneurysms, [2] balloon remodeling for wide neck aneurysms, [3] stent remodeling for large and giant wide neck aneurysms or, [4] therapeutic occlusion for aneurysms unsuited for selective treatment.

The devices used for endovascular procedures in our hospital are purchased through public licitation. The coils used were GDC (Boston Scientific, Fremont, Calif) and Sapphire (ev3, Irvine, Calif). Remodeling balloons were Sentry (Boston Scientific), Hyperglide and Hyperform (ev3). Stent remodeling was performed with Neuroform3 (Boston Scientific).

DSA was performed 6, 18 and 36 months after the treatment. At the time of each angiographic control, a clinical assessment was conducted.

Angiographic occlusion rate were graduated as: complete (class-I), neck-remnant (class-II) or incomplete (class-III) according to the Raymond's classification<sup>10</sup>. They were clinically evaluated according to the modified Rankin's scale (mRS). After inclusion of all patients in the study, we have tried to contact each one of them by telephone to assess their clinical condition.

At the end of the 36-month period, in the absence of recurrence, the patient was discharged. For major recurrences, a retreatment was performed. In our casuistic, all aneurysms with major recurrences were retreated.

Factors possibly related to complications were analyzed such as: patients age, aneurysm size and neck size, and type of treatment, as well as factors possibly related to recurrence such as: unsatisfactory angiographic result, aneurysm size and neck, and type of treatment. Statistical analyses were performed using Fisher's exact test, with a 5% significance level.

## RESULTS

### Patients and aneurysms

From August 2005 to November 2008, 137 saccular aneurysms were treated in 106 patients, 101 unruptured in 75 patients and 36 aneurysms in 31 patients were treated during the acute phase of rupture. Patients included

**Table 1.** Patients.

Age group	
<29 years	3 (2.8%)
30 to 39 years	10 (9.4%)
40 to 49 years	23 (21.7%)
50 to 59 years	36 (34%)
60 to 69 years	23 (21.7%)
≥70 years	11 (10.4%)
Gender	
Female	84 (79.2%)
Male	22 (20.8%)
Ruptured / Unruptured	
Unruptured	75 (70.8%)
Ruptured	31 (29.2%)

**Table 2.** Aneurysms.

Size	
<7 mm	42.3% (58)
7-12 mm	34.3% (47)
13-24 mm	10.2% (14)
≥25 mm	13.1% (18)
Neck	
≤4 mm	39.4% (54)
>4 mm	60.6% (83)
Location	
Anterior circulation	
Acom	7.3% (10)
Pericallosal artery	1.5% (2)
MCA	9.5% (13)
Anterior choroidal artery	1.5% (2)
ICA bifurcation	2.9% (4)
Ophthalmic artery	15.3% (21)
Pcom	18.2% (25)
Superior hypophyseal artery	10.2% (14)
Cavernous segment	13.1% (18)
Persistent trigeminal artery	0.7% (1)
Posterior circulation	
Basilar tip	10.9% (15)
Basilar trunk	3.6% (5)
PICA	2.2% (3)
Posterior cerebral artery	1.5% (2)
Superior cerebellar artery	1.5% (2)
Treatment strategy	
Simple technique	46% (63)
Balloon remodeling	38% (52)
Stent remodeling	10.9% (15)
Therapeutic occlusion	5.1% (7)

Acom: anterior communicating artery; MCA: middle cerebral artery; ICA: internal carotid artery; Pcom: posterior communicating artery; PICA: posterior inferior cerebellar artery.

84 female and 22 male, their ages ranging from 22 to 80 years (mean age, 54 years) (Table 1).

A hundred and ten aneurysms were located in the anterior (80.3%) and 27 (19.7%) in the posterior circulation; 18 (13.1%) in the cavernous segment, 35 (28.5%) were paraclinoid and only 13 (9.5%) were located in the middle cerebral artery (MCA) and 10 (7.3%) in the anterior communicating artery (Acom).

We found 58 (42.3%) small aneurysms (<7 mm), 47 (34.3%) medium (7-12 mm), 14 (10.2%) large (13-24 mm) and 18 (13.1%) giant (≥25 mm). The mean-size was 10.8 mm. Out of the 101 unruptured aneurysms, 41 (40.6%) were small, 29 (28.7%) medium, 13 (12.9%) large, and 18 (17.8%) giant. Among the 36 ruptured aneurysms, 17 (47.2%) small, 18 (50%) medium, and 1 (2.8%) large. Data regarding aneurysms characteristics and locations are demonstrated in Table 2.

### Treatment strategy

Sixty three aneurysms (46%) were treated with coils alone, 52 (38%) with balloon remodeling, 15 (10.9%) with stent remodeling and 7 (5.1%) with therapeutic occlusion (Table 2). Out of the 101 unruptured aneurysms, 33 (32.7%) were treated with coils alone, 46 (45.5%) with balloon remodeling, 15 (14.9%) with stent remodeling and 7 (6.9%) with therapeutic occlusion. Among the 36 ruptured aneurysms, 30 (84.2%) were treated with coils alone, and 6 (15.8%) with balloon remodeling.

### Complications

There were 9 (6.6%) technical complications, 6 (4.4%) asymptomatic and 3 (2.2%) symptomatic. Complications were thromboembolic for 5 aneurysms, stretched coils for 2, rupture for 1 and infected hematoma at the puncture site for 1.

No technical complications occurred for aneurysms treated with stent remodeling or therapeutic occlusion. Four (7.7%) technical complications occurred in the group of aneurysms treated with balloon remodeling and 5 (7.9%) in the group treated with coils alone.

Aneurysm ( $p=0.7138$ ) or neck size ( $p=0.3165$ ), as well as treatment strategy ( $p=0.8674$ ) did not influence the complication rates as shown in Table 3.

Clinical complications occurred in 6 (5.7%) patients among the 106, 3 (2.8%) transitory and 3 (2.8%) permanent. Two permanent clinical complications were due to ischemia related to thromboembolic event and a third one due to a stretched coil in a patient with ruptured aneurysm who was kept under antiplatelets, and had a hemorrhagic complication during a ventricular shunt placement.

There were no difference in terms of clinical complication rates among the age groups ( $p=0.8874$ ) (Table 4).

**Table 3.** Technical complications.

	Complications % (n)
Technical complications	6.6% (9)
Symptomatic	2.2% (3)
Asymptomatic	4.4% (6)
Aneurysm size	
<7 mm	8.6% (5)
7-12 mm	6.4% (3)
13-24 mm	7.1% (1)
≥25 mm	0% (0)
	p=0.7138
Neck size	
≤4 mm	9.3% (5)
>4 mm	4.8% (4)
	p=0.3165
Treatment strategy	
Coils alone	7.9% (5)
Balloon remodeling	7.7% (4)
Stent remodeling	0% (0)
Therapeutic occlusion	0% (0)
	p=0.8674

### Clinical results

Out of the 75 patients harboring 101 unruptured aneurysms, 72 (96%) were independent at the admission (mRS 0-2). Upon hospital discharge, there was clinical deterioration in 1 patient (1.3%).

Clinically, 61 patients (81.3%) were evaluated once, 22 (29.3%) twice and 4 (5.3%) three times (mean follow-up, 12.1 months). Comparing to admission, there was clinical deterioration in 1 patient who became dependent, and improvement of 1 patient who became independent.

Telephone interviews were possible for 74 (98.7%) of the patients harboring unruptured aneurysms (mean follow-up, 22 months), where 70 (94.6%) were independent. Comparing to admission, one patient became independent, and one patient continued to be dependent. Another patient became dependent after meningioma surgery and one died of heart attack.

Subarachnoid hemorrhage for ruptured aneurysms, was graded as Fisher 1 for 1 (3.2%) patient, 2 for 4 (12.9%) patients, 3 for 7 (22.6%) and 4 for 19 (61.3%). According to Hunt and Hess's scale (HH), 19 (61.3%) were in good grade (HH 1-3) and 12 (38.7%) bad grade (HH 4-5).

At discharge, 16 patients (51.6%) were independent, 6 (19.4%) dependent and 9 (29%) died.

Among the 19 patients in good clinical conditions, 15 (78.9%) were independent at the hospital discharge, 2 (10.5%), were dependent and 2 (10.5%) died, whereas among the 12 patients in poor conditions, 1 (8.3%) was independent at the time of discharge, 4 (33.3%) were

**Table 4.** Clinical complications.

	Complications % (n)
Clinical complications	5.7% (6)
Permanent	2.8% (3)
Transitory	2.8% (3)
Age	
<40	0% (0)
40-49	4.3% (1)
50-59	8.3% (3)
60-69	4.3% (1)
≥70	9.1% (1)
	p=0.8874

**Table 5.** Major recurrences.

	Major recurrences % (n)
Total	8.2% (8)
Immediate result	
Class I	2.4% (2)
Class II	50% (4)
Class III	40% (4)
	p<0.0001
Aneurysm size	
<7 mm	0% (0)
7-12 mm	3.3% (1)
13-24 mm	16.7% (2)
≥25 mm	33.3% (5)
	p<0.0001
Neck size	
<4 mm	0% (0)
≥4 mm	13.1% (8)
	p=0.0241
Treatment strategy	
Coils alone	10.2% (4)
Balloon remodeling	10.0% (4)
Stent remodeling	0% (0)
Therapeutic occlusion	0% (0)
	p=0.8674

dependent and 7 (58.3%) died. Among the 31 patients treated in this group, 16 (72.7% of survivors) were clinically evaluated once, 8 (25.8%) twice and 1 (3.2%) three times and 14 were independent (mean follow-up, 14.5 months).

All of the 22 surviving patients after discharge could be contacted by telephone (mean follow-up, 21.5 months). Eighteen (58.06%) were independent, 2 dependent and 2 died of clinical complications. Among the 19 patients in good conditions, only 1 was dependent, representing 84.2% of good results. No patient had any rebleeding episode after aneurysm treatment.

### Angiographic results and follow-up

Angiographic result class I was obtained at the end of treatment for 118 aneurysms (86.13%), class II for 9 (6.57%) and class III for 10 (7.30%).

Angiographic controls were carried out for 97 aneurysms (76.98% of the surviving patients) (mean follow-up, 12.3 months). Thirty-six aneurysms (26.28% of total) were controlled twice and 7 (5.11%) three times.

Among the 97 controlled aneurysms, 8 (8.25%) were retreated. As all major recurrences were retreated, this group was considered for analysis. No complications occurred in the retreatments.

Retreatment had strong correlations with immediate angiographic result ( $p < 0.0001$ ), aneurysm size ( $p < 0.0001$ ) and neck size ( $p = 0.0241$ ), as shown in Table 5.

No retreatment was required for the 13 aneurysms treated by stent remodeling or for the 5 aneurysms treated by therapeutic occlusion. Among the 39 aneurysms treated by coils alone, 4 (10.3%) required retreatment; among the 40 treated by balloon remodeling, 4 (10%) required retreatment, without statistical relevance ( $p = 0.8518$ ). However, when only large and giant aneurysms were analyzed, we verified that 4 (66.7%) of the 6 aneurysms treated by coils alone and 3 (42.9%) of the 7 treated by balloon remodeling required retreatment. None of the 9 aneurysms treated with stent remodeling, or of the 5 aneurysms with therapeutic occlusion, required retreatment. The treatment was more stable for stent remodeling and therapeutic occlusion in this group ( $p = 0.0061$ ).

### DISCUSSION

Representing a series of most non-surgical, a large number of our patients were older than 60 years-old (32.1%). Frequent locations such as MCA and Acom were rarely found, and difficult surgical locations were more common, such as posterior circulation, paraclinoid and cavernous aneurysms. Among the patients treated during the acute phase, 38.7% presented poor clinical condition.

There were a large number of aneurysms treated with balloon (38%) and stent remodeling (10.9%). In the group of unruptured aneurysms, only 32.7% were treated with coils alone, 45.5% with balloon remodeling, 14.9% with stent and 6.9% with therapeutic occlusion.

The first series available in the literature report on the results of aneurysm treatment using only the simple technique, restricted to small neck aneurysms. After the introduction of balloon remodeling by Moret<sup>6</sup>, the embolization of wide-necked aneurysms became possible in safe conditions. Stent remodeling was initially performed with balloon expandable stents, with high complication rates<sup>7</sup>. Self-expandable stents adapted for intracranial circulation have recently shown better results<sup>8</sup> and became an important device in the treatment of intracranial aneurysms.

The therapeutic occlusion of the ICA was described in 1974<sup>9</sup> to deal with complex aneurysms. The occlusion test protocol varies markedly in the literature. We used the angiographic test occlusion described by Abud et al.<sup>11</sup>, without clinical evaluation.

The evaluation of the endovascular treatment of unruptured aneurysms, in the recent ATENA study<sup>12</sup>, presented a proportion of endovascular techniques similar to ours, in which 98.4% of the aneurysms were selectively treated, 54.5% with coils alone, 37.3% with balloon remodeling and 7.3% with stent remodeling.

According to our results, thromboembolic events were the most frequent complication, while the hemorrhagic ones were rare.

Thromboembolic complications incidence ranges between 2.5% and 11% in the literature, with clinical consequences in 2.5% to 5.5% of the patients<sup>13,14</sup>.

Embolic events related to embolization were initially treated with thrombolytic agents, with disastrous consequences to patients with ruptured aneurysms<sup>4</sup>. Antiplatelets, abxycimab<sup>15</sup> and tirofiban<sup>16</sup>, have been recently introduced dealing with these complications with good results.

Aneurysm perforation is the most feared complication; however, it does not always have serious consequences.

In a meta-analysis of 17 retrospective studies<sup>17</sup>, it was found a higher risk of perforation for ruptured aneurysms (4.1%) compared to unruptured ones (0.5%), leading to a morbi-mortality of 38% and 29% respectively.

We have found no statistically significant differences in terms of complications for the different techniques. No permanent complications occurred in the groups of aneurysms treated with stent remodeling or therapeutic occlusion, but the small number of patients included in these groups should be considered. The rates of technical complications were similar for aneurysms treated with coils alone and balloon remodeling.

In Spelle's<sup>18</sup> recent review of the available publications on the endovascular treatment of unruptured aneurysms, the morbidity rate associated with procedures ranged between 3 and 6%, with 1.5% mortality. In the ATENA study<sup>12</sup> the morbidity-mortality rates were 1.7 and 1.4% respectively. In our study we found 1.3% permanent morbidity and 0% mortality related to the procedures for unruptured aneurysms.

In the ISAT study<sup>4</sup>, 88% of the included patients were in good conditions and 75% were independent after treatment. These findings are similar to our population of ruptured-aneurysm patients in good conditions, in which 78.9% were independent at the discharge and 84.2% in the follow-up.

The incidence of angiographic recurrence varies in

the literature, between 14.7% and 33.6%<sup>19,20</sup>. Retreatment rate is more stable, around 10%<sup>20,21</sup>, and is related to larger recurrences.

Piotin<sup>19</sup> published a study about aneurysm recurrence, evaluating 255 selectively embolized aneurysms with at least one angiographic control. Seventy-three aneurysms (28.6%) presented recurrence and 14 (5.5%) were retreated. The length of follow-up was the most important factor.

Raymond<sup>20</sup> studied 501 ruptured aneurysms, and found recurrence in 33.6% of the cases. Major recurrences were found in 20.7% and half of them were retreated (10.2%). The factors implied with recurrence were aneurysms treated in the acute stage, aneurysm size, neck size, incomplete immediate result and follow-up duration.

In the angiographic follow-up of the ISAT study<sup>22</sup>, retreatment was necessary for 10.6% of the patients that were submitted to control angiograms.

If only large and giant aneurysms are considered, which represent a challenge for the endovascular technique due to their high rate of recanalization<sup>23</sup>, we have found that treatment with stent remodeling and therapeutic occlusion of the ICA were statistically more stable than simple technique and balloon remodeling. However, these groups were smaller than the groups of aneurysms treated with balloon remodeling or by simple techniques. The development of new devices such as the flow-diverter stents may improve the stability over time in these groups<sup>24</sup>.

Our retreatment rate was 8.2% considering the 97 aneurysms that were submitted to at least one angiographic control and is similar to other results in the literature.

Although recurrence rate is always brought to attention in the discussion of endovascular embolization, it is well established in the literature that complications related to retreatment are rare.

A recent study<sup>25</sup> reported 100 retreated aneurysms in 99 patients and found thromboembolic events in 3 procedures, without clinical implications.

The contribution of endovascular therapy in dealing with cerebral aneurysms is undeniable. Our series of patients with high surgical risk showed good results and reveals that, in our context, embolization can be safely applied.

In conclusion, endovascular treatment is a viable option within the Brazilian public health care system and must be taken into account when treatment options are discussed for such patients. The results for our series of predominating non-surgical aneurysms are similar to those available in current publications.

Aneurysm size, neck size, patient age and treatment strategy did not alter the complication rates.

Sac and neck dimensions as well as immediate angiographic results are related to recurrence.

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