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Follow-up of endovascular treatment of direct carotid-cavernous fistulas

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Abstract
Introduction Direct carotid-cavernous fistula (CCF) is a direct communication between the internal carotid artery (ICA) and the cavernous sinus. Some patients treated with detachable balloons develop pseudoaneurysms or present with a true aneurysm recanalization in the cavernous ICA with poorly known long-term radiological and clinical progression. The objective of the present study was to evaluate the long-term clinical and radiological progression of patients treated with detachable balloons.
Methods The present study evaluated 13 patients previously treated for direct CCF by an endovascular approach.
Results The follow-up period ranged between 19 and 128 months. Ophthalmological evaluation demonstrated alterations in eight patients (61.5%). All of these alterations were already present from the moment of the treatment and displayed no signs of progression. Cranial magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were performed in all patients, and 11 pseudoaneurysms were demonstrated in ten of the 11 patients in whom ICA patency had been preserved. Five patients were submitted for cerebral digital subtraction angiography (DSA) to characterize the pseudoaneurysms previously observed on MRA studies, with no significant differences in morphology, size, aneurismal neck, and number of lesions.
Conclusion Endovascular treatment of direct CCF with detachable balloons has been shown to be a long-term effective and stable therapeutic method. The authors found asymptomatic pseudoaneurysms in 91% of cases where the ICA patency was preserved. MRI and MRA demonstrated an accuracy similar to that of DSA in the diagnosis of pseudoaneurysms of cavernous ICA.

Keywords Carotid disease · Fistulas · Magnetic resonance imaging · MR angiography · Outcomes

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Introduction

Direct carotid-cavernous fistulas (CCF) are characterized by a direct connection between the internal carotid artery (ICA) and the intraluminal space of the cavernous sinus (CS) and, according to Barrow [1], they are classified as type A fistulas. In 1974, Serbinenko [2] described the endovascular approach used for the treatment of direct CCFs, utilizing detachable balloons as a therapeutic alternative to surgery. With the development of endovascular techniques and materials, this approach has become the best therapeutic option and has achieved high rates of cure with low morbidity [3, 4]. The main objective of the endovascular treatment is the selective occlusion of the fistula by means of detachable balloon deployment. However, the fistula isolation by means of ICA occlusion is considered for specific cases where the fistula point cannot be selectively occluded. The presence of pseudoaneurysms in the ICA cavernous segment observed at post-treatment follow-up may occur in about 30-44% of patients

[5]. Such pseudoaneurysms may develop asymptomatically and become large enough to compress the cranial nerves related to the CS, or even determine direct CCF recanalization [5]. A few studies in the literature describe long-term, clinical, and radiological follow-up of patients submitted for endovascular treatment for direct CCF [5]. In the present study, we aimed to evaluate the long-term clinical and radiological follow-up of patients treated with detachable balloons.

Casuistic

The present study was developed from January 2006 to March 2007, from the evaluation of 13 patients submitted for endovascular treatment for direct CCF at the Hospital das Clínicas/Incor and the Hospital São Paulo (UNIFESP), in São Paulo, SP, Brazil, from October 1997 to February 2006. All patients were treated with transarterial detachable latex balloons (GOLDBAL1 7×10 mm, GOLDBAL2 7×20 mm, GOLDBAL3 9×11 mm and GOLDBAL4 9×16 mm; Balt Extrusion, Paris, France) by femoral approach with 8F introducers and seaths. The balloons were filled with iso-osmotic, water-soluble contrast material. All procedures were performed under general anesthesia and under intravenous heparin administration (an initial bolus of 80 U/Kg followed by 18 U/Kg/h).

Methods

Inclusion criteria

1. Patients with imaging studies or clinical reports proving the diagnosis of direct CCF.
2. Patients submitted for endovascular treatment with detachable balloons for direct CCF.
3. Patients whose pre- and post-treatment clinical histories were available.
4. Patients >18 years of age.

Clinical evaluation

All of the patients were interviewed by a single neuroradiologist, with a focus on the previous clinical history and on the presence of ocular signs or symptoms such as orbital bruit, conjunctival hyperemia, chemosis, diplopia, and proptosis at the time of treatment and at the follow-up. The ophthalmological evaluation of the patients was performed at the specialized unit of UNIFESP in São Paulo, SP, Brazil, and was principally aimed at ruling out the presence of other ocular pathologies.

Evaluation of previous imaging studies

Previous diagnostic and interventional digital subtraction angiography (DSA) images available were analyzed by two neuroradiologists with 5 and 20 years of experience. The main findings considered were the following: (a) presence of aneurysms and pseudoaneurysms in the ICA cavernous segment as well as the morphology, size, neck, and number of lesions; (b) presence of fistulas; and (c) venous drainage pattern.

Follow-up imaging studies

Initially, the patients were submitted for magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the cavernous sinus and orbital regions, in compliance with the study protocol including the following sequences:

- TOF-3D: TR 36 ms; TE 4.47 ms; FOV 200 mm; RFOV 93.8 mm; slice thickness 0.9 mm ; matrix size 264×512;
- 3D, SE (spin-echo) T1-weighted: TR 2,000 ms; TE 3.42 ms; FOV 256×256 mm; slice thickness 1×1×1 mm; resolution 256×256;
- Coronal, TSE (turbo spin-echo) T2-weighted: TR 4,000 ms; TE 88 ms; FOV 220 mm; RFOV 80×100 mm; slice thickness 4 mm; GAP 0.4 mm; turbo factor 11; resolution 205×320.
- 3D CISS: TR 8.65 ms; TE 4.33 ms; FOV 180 mm; RFOV 180 mm; slice thickness 1 mm; resolution 256×256.

These studies were performed using a Siemens Sonata 1.5T, 40 mT gradient equipment (Siemens Medical Solution, Erlangen, Germany), at the UNIFESP Department of Diagnostic Imaging. The acquired images were analyzed by the already mentioned neuroradiologists. The main findings considered were the following: (a) presence of aneurysms or pseudoaneurysms in the ICA cavernous segment as well as morphology, size, neck, and number of lesions; (b) signs suggestive of the presence of fistulas, such as alterations in the caliber of the orbital veins and of the CS, edema of the intraconal muscle, and proptosis. The radiological findings were compared with those of the previous images and were correlated with the clinical findings. Cerebral DSA was performed in the patients who: (a) presented clinical and/or radiological findings suggestive of fistula recanalization; (b) at MRA, presented aneurysms or pseudoaneurysms in the ICA cavernous segment that had not been observed in the previous imaging studies; and (c) presented radiological signs of the progression of morphological alterations (aneurysms or pseudoaneurysms) of the cavernous ICA, as compared with previous imaging studies. Such patients underwent cerebral digital subtraction angiography of the internal and external carotid and vertebral arteries. All of

the DSA studies were performed by a single neuroradiologist with 5 years of experience and using Phillips Integris V 5000 equipment (Phillips Medical Systems, Holland) with 1,024×1,024 resolution, at the UNIFESP. The images were analyzed by the two previously mentioned neuroradiologists. The main findings considered were the following: (a) presence of aneurysms or pseudoaneurysms in the ICA cavernous segment as well as morphology, size, neck, and number of lesions, (b) presence of fistulas, and (c) venous drainage pattern.

The present study was approved by the Committee for Ethics in Research of Universidade Federal de São Paulo, and all of the patients signed a term of free and informed consent.

Results

From January 2006 to March 2007, the authors evaluated 13 (seven male and six female) patients in the age range between 19 and 59 years (mean, 41.7 years). In eight patients, the etiology was related to trauma. Six of these patients were men. Spontaneous fistulas were found in five patients, four of whom were women. Internal carotid artery patency was preserved in 11 patients (84.6%). Therapeutic occlusion of the ICA was performed in two cases (15.4%; cases 2 and 7) after unsuccessful attempts of fistula selective occlusion. These patients presented with functional exclusion of the ICA due to the major steal of flow and the balloon occlusion test was not necessary. In both patients, the double-balloon technique was used for the occlusion of the ICA. One case presented premature balloon deflation (case 5) 24 h after treatment and a second procedure was promptly and successfully performed. No premature balloon detachment was observed in this study. The follow-up period ranged between 19 and 128 months (mean, 66.2 months). Table 1 shows the main data for the cases included in the present study. Ophthalmological evaluation demonstrated alterations in eight patients (61.5%). The authors discovered ophthalmoparesis in six patients, five of which had a traumatic etiology (cases 2, 3, 4, 7, and 9) and only one case of spontaneous etiology (case 11). The VI nerve was involved in five cases, and the III nerve in two cases. However, only two patients (cases 7 and 9) presented visual complaints. Complete amaurosis was identified in three cases (cases 4, 10, and 13). According to data regarding the patients' clinical history, all of the ophthalmological findings were already present from the time of treatment, and there were no complaints suggesting the progression of these findings up until the moment of the ophthalmological evaluation. Table 2 shows the distribution of these findings according to their etiology. MRI and MRA were performed in all of the patients. Among them, 12 patients did not present any radiological findings suggestive of fistula recanalization. In case 9, the female patient presented conjunctival hyperemia during abdominal stress and cough, as well as dilatation of the orbital veins and proptosis on MRI. In this case, DSA demonstrated CS thrombosis and consequential redirectioning of the blood flow through the orbital and facial veins (Fig. 1). DSA and MRA also demonstrated a decrease in the size of a small pseudoaneurysm that had been observed in the previous DSA study. Among the 11 patients in whom ICA patency had been preserved, ten (91%) presented pseudoaneurysms of the cavernous ICA (cases 1, 3, 4, 5, 6, 9, 10, 11, 12, and 13). The authors found 11 lesions with sizes ranging between 2 mm×2 mm and 29×16 mm at their largest axes. Five of these patients (cases 1, 4, 5, 11, and 12) were submitted for DSA to characterize the pseudoaneurysms previously observed at MRA, with no significant difference as to morphology, size, neck, and number of lesions. In case 4, the patient presented two pseudoaneurysms (Fig. 2).

Discussion

The endovascular approach using detachable balloons was performed in all the patients included in the present study. Internal carotid artery patency preservation was achieved in 11 cases (84.6%), and none of the patients progressed with fistula recanalization, demonstrating the long-term stability of this method.

The high rate of ICA patency preservation and the treatment stability achieved with this technique corroborate the efficacy of the method and are compatible with data reported in the literature [4–6]. New techniques involving the utilization of intracranial metal microcoils, biological glues, remodeling balloons, and stents are applied in a small number of patients, with good outcomes being reported in the literature [7–10]. In spite of the development of these endovascular techniques, detachable balloons are still widely utilized, especially in centers with restricted financial resources, considering the lower cost of this technique compared with the cost of the above-mentioned most recent techniques.

The ophthalmological examination revealed alterations in more than half of the patients included in the present study (61.5%), and most of these alterations were related to involvement of the cranial nerves III and VI. Cranial nerve lesions were most frequently observed in patients who had undergone trauma (75%, Table 1). This finding suggests that cranial nerve lesions are determined by the occurrence of fractures in the region of the cavernous sinus related to deceleration mechanism, present in cases of trauma classically described as responsible for the ICA wall laceration [6]. In the reviewed series [3–6], the rate of transitory and

Table 1 Demographic, treatment data, and ophthalmological examination findings.

Case	Age (years)	Sex	Etiology	Follow-up months	Ophthalmological study
1	42	Female	Spontaneous	128	Normal
2	51	Female	Traumatic	111	Ophthalmoparesis (III and VI nerves)
3	52	Male	Traumatic	103	Ophthalmoparesis (VI nerves)
4	31	Male	Traumatic	86	Ophthalmoparesis (III and VI nerves) Amaurosis
5	36	Female	Spontaneous	85	Normal
6	37	Female	Spontaneous	76	Normal
7	37	Male	Traumatic	73	Ophthalmoparesis (VI nerve)
8	59	Female	Traumatic	58	Normal
9	42	Female	Traumatic	47	Ophthalmoparesis (VI nerve)
10	19	Male	Traumatic	29	Amaurosis
11	44	Female	Spontaneous	15	Ophthalmoparesis (VI nerve)
12	34	Male	Traumatic	31	Normal
13	59	Male	Spontaneous	19	Amaurosis

permanent lesion incidence in cranial nerves is lower than 1%. Such results disagree with those of the present study. However, among the six patients with ophthalmoparesis diagnosed in the ophthalmological evaluation, only two presented visual complaints. This fact can partially explain the abovementioned disagreement, considering that the reviewed series do not specify the criteria adopted to classify a patient as symptomatic. Thus, patients with small extrinsic ocular motricity deficits that do not impair their daily activities may be considered as asymptomatic. However, the authors did not observe post-treatment ophthalmological alterations in the patients submitted for endovascular treatment. Thus, the authors do not associate such alterations with the aneurysms and pseudoaneurysms found at the radiological follow-up performed in the present study, which will be discussed henceforth.

The evaluation by MRI and MRA was performed in all of the patients included in the present study and revealed 11 pseudoaneurysms of the ICA cavernous segment in ten of the 11 patients whose ICA patency had been preserved, all of whom were asymptomatic. A few data are available on the incidence and natural course of these pseudoaneurysms.

Table 2 Ophthalmological findings—distribution according to etiology.

Ophthalmological Study		
Etiology	Normal no. (%)	Altered no. (%)
Traumatic	2 (25)	6 (75) ophthalmoparesis—5; ophthalmoparesis+amaurosis —1;amaurosis—1
Spontaneous	3 (60)	2 (40) ophthalmoparesis—1; amaurosis—1
Total	5	8

According to some studies in the literature [4, 5, 11], their incidence ranges between 30% and 44%, with most of them being asymptomatic. The occurrence of these pseudoaneurysms is related to ICA wall failure following deflation of the balloon placed at the fistula point [11]. In spite of this significant incidence, recommendations on follow-up and the eventual treatment of such complications have yet to be clearly described in the literature. According to the authors of these reviewed series, such pseudoaneurysms present a low potential for fatal complications because of their extradural location. Additionally, according to these authors, pseudoaneurysms may progress as follows: growth determining compression of nervous structures in the CS, growth and rupture determining fistula recanalization, growth determining the occurrence of distal embolic phenomena, asymptomatic progression, and even size regression. The authors did not identify any late compressive signs or symptoms, fistula recanalization, or embolic phenomena in the patients included in the present study. Lewis et al. [11] followed-up 76 patients for a period ranging from 1 to 15.5 years. The authors found neither clinical deterioration nor fistula recurrences in their series. However, only 14 of these patients were systematically followed-up with cranial MRI and MRA. Pseudoaneurysms were found in 12 of them, with only one symptomatic patient presenting distal embolic phenomena. These results are similar to the ones observed in the present study. On the other hand, the actual incidence of pseudoaneurysms could not be demonstrated by Lewis, considering that the majority of their patients were not submitted for a systematic radiological investigation. The study developed by Lewis et al. also identified pseudoaneurysm size regression in two cases, similarly to the study developed by Jun-Seok et al. [12] and to the case 9 described in the present study. In the past, the management of such

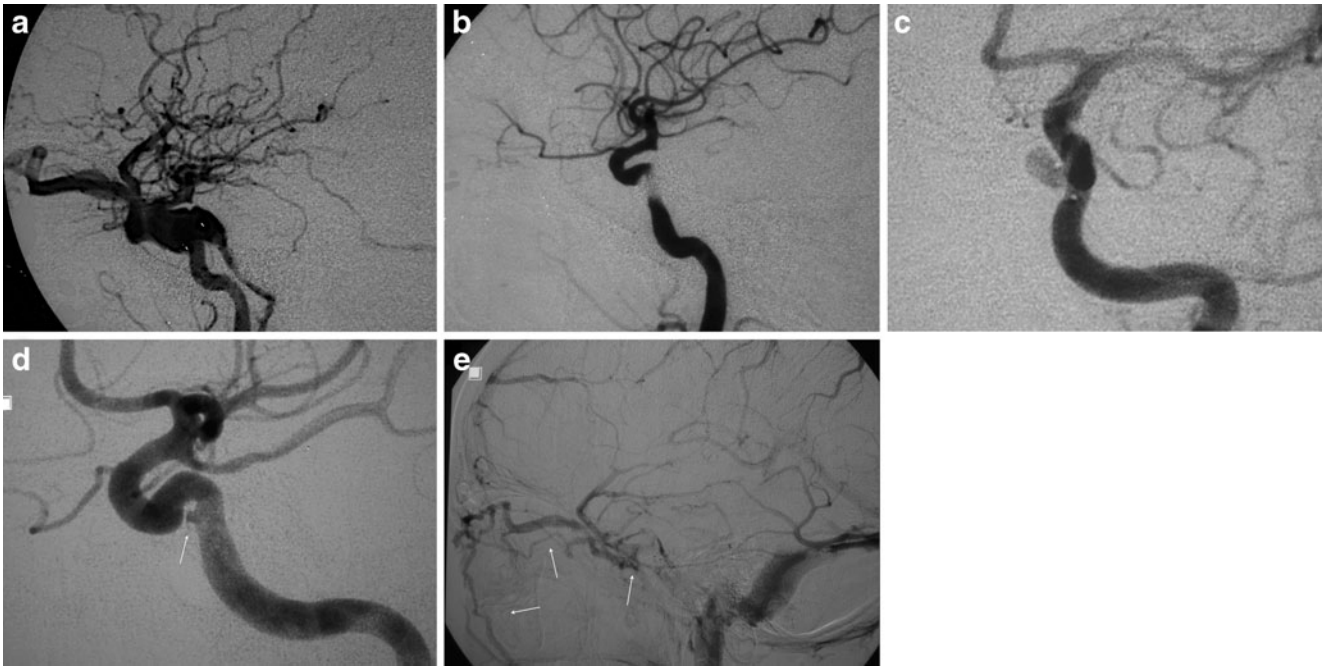

Fig. 1 Patient 9. **a** Lateral DSA image of the left common carotid artery acquired in January 2004 showing the DCCF **b** lateral DSA image of the left common carotid artery showing the immediate post-treatment result. **c** Frontal DSA view of left common carotid artery acquired in May 2004, showing a stable occlusion of the fistula and a small pseudoaneurysm in the cavernous segment **d** lateral DSA image of the left ICA acquired in December 2007, showing a regression in the size of pseudoaneurysms (*arrow*) in the left cavernous ICA (**e**) lateral DSA image at the venous phase of the left ICA, demonstrating redirectioning of the venous return of the SMCV through the SOV, angular, and facial veins (*arrows*)

pseudoaneurysms was carried out with detachable balloons [13, 14]. Presently, the successful treatment for both intra- and extradural intracranial pseudoaneurysms by means of different techniques has been reported in the literature [15–17], usually involving the utilization of intracranial covered stents [15, 16]. However, these new as well as less modern techniques are not free from risks and require further clinical and follow-up studies for their validation. Additionally, the poor symptomatology of the majority of pseudoaneurysms in the cavernous ICA, in association with the possibility of spontaneous regression observed in the present study as well as in the abovementioned reviews, suggests that the benign behavior of these lesions does not indicate the necessity of an aggressive approach. The use of anticoagulant and antiplatelet agent therapy had been poorly described for the management of this type of pseudoaneurysm [18, 19]. However, we should consider the very low frequency of new cerebral ischemic events in patients with dissecting lesions of the ICA despite the type of antithrombotic treatment imposed and the risks of hemorrhagic complications [20]. We did not institute any treatment in our patients because they had not experienced neurological ischemic events by the clinical follow-up.

In the two cases in the present study where the ICA was occluded, the authors did not observe the development of "de novo" aneurysms. Such aneurysms may develop

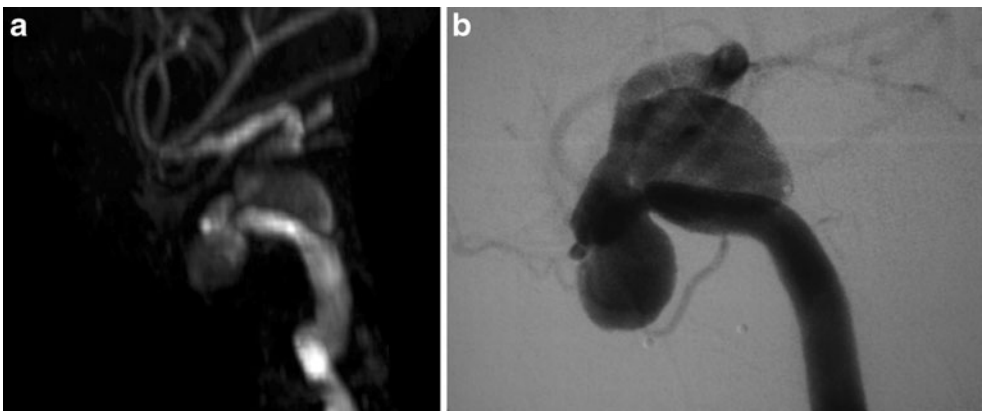

Fig. 2 Patient 4. **a** 3D-TOF MRA image with MIP reconstruction showing two pseudoaneurysms in the left cavernous ICA and areas of segmental decrease in the artery caliber **b** oblique DSA view of the left ICA demonstrating the pseudoaneurysms previously observed at MRA

following occlusion of one of the ICAs, most frequently in the anterior communicating artery complex, as a result of the increased blood flow in this region [21].

In the present study, cerebral DSA was performed in six patients. In case 9 described in the topic "Results" section, such a study was indicated because of the presence of symptoms suggestive of fistula recanalization and radiological signs suggestive of a change in the pattern of orbital vein drainage as well as a regression in the size of a pseudoaneurysm that had been observed previously in radiological studies. The DSA demonstrated the redirectioning of the superficial middle cerebral vein (SMCV) drainage caused by the CS occlusion and characterized in detail the regression in size of the pseudoaneurysm of the cavernous ICA. In this particular case, the DSA study played a relevant role in the characterisation of the venous drainage pattern, which was essential for ruling out the presence of fistula recanalization.

Presently, dynamic MRA [22] already allows an accurate, dynamic evaluation in cases of cerebrovascular diseases. However, the availability of this method in the author's environment remains poor. In cases 1, 4, 5, 11, and 12, DSA was indicated because of the presence of focal dilatation of the cavernous ICA that had not been observed in previous studies. By comparing MRA and DSA findings in these cases, the authors did not find any significant differences in relation to morphology, size, neck, and number of pseudoaneurysms characterized by other imaging methods. The presence of metal material in the balloon valve in the CS region did not play a significant role in the image acquisition, as demonstrated by the present study. These observations corroborate the MRI and MRA value obtained in the follow-up of these cerebrovascular pathologies and are compatible with the pertinent literature [23], considering the non-invasiveness, low risk, and lower cost of MRI and MRA as compared with DSA in addition to the equivalent accuracy. Agreeing to this discussion, we consider necessary to systematically perform a MRA after 6 months to 1 year in all patients submitted for treatment. The frequency of subsequent radiological follow-up should be guided by these primary imaging findings in association with the clinical surveillance. The DSA should be reserved for patients with symptomatic pseudoaneurysms.

Conclusion

The endovascular approach for the treatment of direct CCF with detachable balloons has been shown to be a long-term, effective, and stable therapeutic method with very low costs. The high incidence of pseudoaneurysms observed in the present study calls attention to the necessity of clinical and radiological follow-up of patients submitted for this technique and highlights the necessity of further studies to clarify their natural progression. MRI and MRA demonstrated an accuracy similar to that of DSA in the diagnosis of pseudoaneurysms of the cavernous ICA.

Conflict of interest statement We declare that we have no conflict of interest.

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