ORIGINAL ARTICLE

Endovascular treatment of symptomatic intracranial stenoses: Short- and long-term results in a single center

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Abstract
Objectives: We present the short- and long-term results of a series of patients with symptomatic intracranial arterial stenoses treated with angioplasty and stenting.

Materials and methods: We reviewed patients with symptomatic intracranial stenoses greater than 50% who were treated with angioplasty, stenting, or both. We recorded demographic data and risk factors (hypertension, diabetes, dyslipemia, ischemic heart disease). We classified all lesions treated according to their location, degree of stenosis, and length. The degree of stenosis was classified as moderate (50–70%) or severe (>70%). In the follow-up, we assessed cerebrovascular accidents, episodes of ischemic heart disease, and deaths in the first 30 days and in later follow-up.

Results: Between 2006 and 2010, we treated 26 patients (21 men and 5 women; age range, 44–79 years; mean age, 63 years) with 29 intracranial lesions. The endovascular procedure (angioplasty + stenting) was successfully performed in 23 cases (92.0%). In the first 30 days after the procedure, 3 (11.5%) patients had adverse effects of vascular origin: 1 stroke, 1 hemorrhage, and 1 death due to thrombosis of the stent. Long-term follow-up (5–46 months) in the 25 patients who survived more than 30 days detected no recurrence of symptoms.

Conclusion: Endovascular treatment of intracranial stenosis is technically feasible. Short-term complications are highly prevalent. No recurrence of symptoms was detected during long-term follow-up.

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KEYWORDS
Arterial stenosis; Endovascular treatment; Angioplasty; Stent; Cerebral arteries


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Endovascular treatment of symptomatic intracranial stenoses

PALABRAS CLAVE
Estenosis arterial; Tratamiento endovascular; Angioplastia; Endoprótesis; Arterias cerebrales

Tratamiento endovascular de estenosis intracraneales sintomáticas: resultados a corto y largo plazo de un único centro

Resumen
Objetivos: Presentamos los resultados a corto y largo plazo de una serie de pacientes con estenosis arteriales intracraneales (EAIC) sintomáticas tratados en nuestro centro mediante angioplastia y endoprótesis.

Material y métodos: Revisión de pacientes con estenosis intracraneales >50% sintomáticas tratados en nuestro centro mediante angioplastia y/o colocación de endoprótesis. Se recogieron los datos demográficos y los factores de riesgo vascular (hipertensión, diabetes, dislipidemia, cardiopatía isquémica). Todas las lesiones tratadas se caracterizaron por su localización, grado y longitud de la estenosis. El grado de estenosis se calificó como moderado (50–70%) o grave (>70%). En el seguimiento se evaluaron los accidentes cerebrovasculares, episodios de cardiopatía isquémica o fallecimientos ocurridos durante los 30 primeros días y en el seguimiento posterior.

Resultados: Entre 2006 y 2010 se trataron 26 pacientes (21 varones y 5 mujeres) con edades comprendidas entre 44 y 79 años (media: 63 años), con 29 lesiones intracraneales. El procedimiento endovascular se realizó con éxito (angioplastia + endoprótesis) en 23 casos (92.0%). En los 30 primeros días postintervención se produjeron tres (11,5%) efectos adversos de origen vascular: un ictus, una hemorragia y un fallecimiento por trombosis de la endoprótesis. El seguimiento a largo plazo se ha realizado sobre 25 pacientes (5–46 meses). No se han detectado recurrencias de la sintomatología.

Conclusión: El tratamiento endovascular de las EAIC es técnicamente factible. Las complicaciones del procedimiento a corto plazo tienen una prevalencia alta. No se ha detectado recurrencia de la sintomatología a largo plazo.

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Introduction

Intracranial artery stenoses (IAS) are one of the causes of stroke and responsible for nearly 5–10% ischemic strokes. The risk to suffer a IAS-induced stroke is close to 8–22% depending on severity and location. The Warfarin-Aspirin Recurrent Stroke Study (WARSS) and Warfarin Aspirin Symptomatic Intracranial Disease Study (WASID) trials showed the poor effectiveness of medical management of IAS. This is one of the reasons why transluminal angioplasty and vascular endoprothesis arise as useful therapeutic tools. Our goal is to reveal the short and long term results of a series of patients with symptomatic IAS treated using angioplasty and endoprothesis.

Materials and methods

We reviewed patients included in a IAS database treated with angioplasty and/or endoprothesis between 2006 and 2010. Approval from the hospital’s Ethical Committee was not needed since it was a retrospective study of patients. Asymptomatic patients incidentally diagnosed with IAS with non-invasive trials (CT-angio and/or MR-angio), or patients who presented with neurologic events with total recovery in the first 24h were initially managed with an aggressive medical treatment through double anti-aggregation therapy—most patients with acetylsalicylic acid and clopidogrel, monitoring of cardiovascular risk factors—hypertension, diabetes, dyslipidemia, and habit changing therapy—smoking cessation, diet and physical exercise. Despite medical therapy symptomatic patients were considered candidates for endovascular treatment.

Demographic data (age and gender) of every patient and vascular risk factors—hypertension, diabetes, dyslipidemia, ischemic heart disease, smoking—were gathered.

Pre-proceeding

All patients were informed of all risks and benefits associated to the proceeding and signed their informed consent forms. A daily pharmacological treatment was initiated with two (2) antiaggregant agents (300 mg of acetylsalicylic acid plus 75 mg of clopidogrel) at least four (4) days before intervention.

Proceeding

General anesthesia was used. Right femoral approach was the preferred approach but for those patients with access issues through femoral approach in which humeral approach was used. Unfractioned heparin was used through the intervention to achieve an activated clotting time (ACT) ≥ 250 s. A 6F Macht carrier stent (Boston Scientific, Natick, MA, USA) was implanted in the cervical internal carotid artery for injuries occurring in the anterior circulation or in the vertebral artery for those occurring in the posterior circulation.

In all injuries treated the location, degree and length of stenosis were determined. Anterior circulation stenosis was regarded as such if located in the intracranial carotid...
artery and in the anterior and middle cerebral arteries initial segments. In the posterior circulation the vertebral artery and basilar trunk extravertebral (V3) and intracranial (V4) extradural segments of the vertebral artery and the basilar trunk were taken into consideration. The degree of stenosis was rated as moderate (50–70%) or serious (>70%) according to criteria from the North American Symptomatic Carotid Endarterectomy Trial (NASCET), comparing the diameter of stenosis to the distal internal carotid artery distal from the injury. Length of stenosis was rated as short (<5 mm), medium (5–10 mm) or large (>10 mm).

Injury was pierced with a 0.12 hydrophilic guide wire (Terumo, Tokyo, Japan) and a Vasco 10 low profile microcatheter (Balt, Montmorency, France). Guide wire was then replaced by a Transend 0.14 interchange wire (Boston Scientific, Natick, MA, USA) onto which a Gateway balloon moved forward (Boston Scientific, Natick, MA, USA). Diameter of the balloon was picked according to the normal diameter of the distal artery affected segment with a length that could cover it all. Balloon then was slowly inflated at a pressure of 1 atm every 15 s until reaching the diameter of the vessel. Balloon was then removed and a Wingspan prosthesis (Boston Scientific, Natick, MA, USA) moved forward. The diameter of prosthesis was picked according to the post-stenotic healthy artery caliber with a length capable of covering at least 3 mm proximal and 3 mm distal to stenosis. After releasing the endoprosthesis angiographic monitoring to confirm the device patency and absence of vascular complications was carried out. The proceeding technical success was considered to be a residual stenosis <20%. All complications occurring during the interventional proceeding were registered—artery perforation, stenotic artery thrombosis or distal embolism.

After completing the proceeding the patient remained 24 h at the Intensive Care Unit. No anticoagulant drugs were administered.

Follow up

Independent neurologists did the follow up of all minor stroke, and major stroke events, acute myocardial infarction and all cause mortality 30 days after the intervention (short-term follow up). The same neurologists did another long term follow up through clinical interviews.

Minor stroke was regarded as an acute neurological process rated ≤3 at the National Institutes of Health Stroke Scale (NIHSS), or without functional disability after 30 days. Major stroke was rated ≥4 at the National Institutes of Health Stroke Scale (NIHSS), and functional disability after 30 days. All causes of death were registered.

Results

Twenty-six patients were treated between 2006 and 2010 (21 males and 5 females) aged 44–79 years (average 63 years) with 29 intracranial injuries. Vascular risk factors can be seen in Table 1.

All patients suffered from strokes or repeated transient ischemic accidents (TIA) relapsed despite medical therapy. Above all injuries were located in the posterior circulation (16 cases, 61.5%) at the vertebral artery V4 segment (8 cases, 30.7%) (Fig. 1) or at the basilar trunk (8 cases, 30.7%) (Fig. 2). Anterior circulation stenoses (10 cases, 38.5%) were located at the intracranial internal carotid (6 cases, 23%, 4 at the intrapetrous segment and 2 at the cavernous segment) (Fig. 3) and at the middle cerebral artery (4 cases, 14.4%).

Degree of stenosis was rated as moderate (12 cases) or serious (14 cases). Length of stenosis was short in 6 occasions, moderate in 7 and long in 13 cases.

Endovascular proceeding was carried out in an attempt to do an angioplasty and implant the endoprosthesis achieving technical success in 23 cases (92%). In two (2) cases angioplasty was done but the endoprosthesis could not be implanted for technical issues. One final patient showed multiple moderate injuries (<70%) at the right vertebral artery intracranial segment which resolved through angioplasty with a fine angiographic outcome.

During the first 30 days three (3) vascular adverse events happened (Table 2). One patient suffered a protuberantial stroke due to the obstruction of the basilar trunk perforating branch maintaining patency of endoprosthesis though. Other patient with stenosis at the middle cerebral artery developed a reperfusion syndrome with intraparenchymatous hemorrhage. Lastly one female patient was not treated with double antiaggregation for being allergic to clopidogrel and died of an acute thrombosis of endoprosthesis. All these events happened during the first 24 h.

There was a long term follow-up of 25 patients (96, 15%) after the first 30 days (Table 3) for at least 5 months and a

<table>
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<td>DM</td>
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<tr>
<td>Dyslipemia</td>
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</tr>
<tr>
<td>Smoker</td>
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</tr>
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<td>Former smoker</td>
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</tr>
<tr>
<td>Ischemic heart disease</td>
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<td>DM: diabetes mellitus; HBP: high blood pressure.</td>
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<td>Hemorrhage</td>
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Figure 1  52-year-old patient who had one ischemic stroke in the left posterior inferior cerebral artery. Stenosis could be identified through arteriography in the left vertebral artery (A) and the basilar trunk (arrow) and was treated with angioplasty and endoprosthesis (B and C).

Figure 2  62-year-old patient who had one vertebro-basilar transient ischemic attack. Angiographic test showed vertebral stenosis (continuous arrow) and one aneurisma (discontinuous arrow) at the beginning of the left posterior inferior cerebral artery (A) which were treated with both endoprosthesis (B) and coiling at the same surgical act.

Figure 3  70-year-old patient who presented with one ischemic attack at the left sylvian territory. Angio-MR test (not shown) showed intrapetrous stenosis confirmed by arteriography (A and B) (arrow) which was treated with angioplasty.
maximum of 3 years and 10 months—an average 1 year and 7 months and a median 1 year and 4 months.

Symptomatology recurrences could not be spotted. Two (2) ischemic strokes in vascular territories different from the IAS treated occurred. In one case with left middle cerebral artery stenosis a minor contralateral carotid stroke occurred. Other patient with a treated vertebrobasilar stenosis suffered a major heart attack at the right middle cerebral artery.

During follow-up there were not any myocardial ischemic events.

Two (2) patients died for other reasons—one of a cerebral lymphoma (8 months after treatment) and the other of a lung neoplasm (6 years after treatment).

**Discussion**

Despite the aggressive medical therapy with double anti-aggregation our symptomatic IAS patients were treated through angioplasty and endoprosthesis. Choice was very thorough: only symptomatic patients with vascular recurrence despite antiaggeregant therapy. Technical success was close to 92% during intervention but there were 3 adverse events during the first 24h. Use of endovascular techniques to treat IAS is very well documented with an average success rate of 96.9% (range 70–100%) and a perioperative morbi-mortality including minor stroke, major stroke and death between 4.4 and 14.4%. Our morbi-mortality was close to 11.5% and similar to the last series published. Both in those series and in our series short term complications occurred during the first days. No new symptomatic events were registered in the long term.

IAS caused nearly 10% of all cerebral strokes with a recurrence rate of 15%, Degree of stenosis is associated to the risk of suffering a stroke or an ITA, so therapy is needed.

Since endovascular therapy of IAS through angioplasty and endoprosthesis shows a high morbi-mortality rate the selection of patients needs to be extremely accurate. In our center endovascular therapy only applies to patients with IAS and clinical relapse; ITA; or stroke despite the antiaggeregant therapy.

Management of IAS has a better prognosis with antiaggeregant drugs than anticoagulants. It was believed that aggressive treatment with double antiaggregation was little effective in the long run in high-degree stenosis (>70%), which could benefit from invasive therapies. But in a recent study morbi-mortality after the interventional proceeding of severe stenoses was 14.7% vs 5.8% of symptomatic events with double antiaggregation. After a 11.9 month follow-up recurrence rates were similar in both subgroups with no statistical differences. Work suggests that patients with severe IAS have a lower risk to suffer strokes than was initially thought.

After neurointerventional therapy double antiaggregation is priority to prevent thromboembolic events. Likely the immediate thrombosis of our patient would not have occurred with it. Platelet function monitoring through the antiaggregation assay is not routine procedure but could add some security to the proceeding since 28% of symptomatic patients having neurointerventional proceedings done are nonrespondents to clopidogrel.

Follow-up of patients took place through clinical interviews led by independent neurologists. We have not found long term symptomatic recurrences in the treated arteries. This is likely due to the size of the sample since larger series show a symptomatic recurrence rate of 4.7%. Nevertheless two (2) strokes were documented in other cerebral vascular territories.

The vessel patency monitoring was controlled through Doppler ultrasound or MR-angio but not with systematic arteriographical assays. Despite confirmation of long term stenosis (range: 0–50%; average: 3.9%), we believe repeat therapy depends on the patient’s symptoms. We disagree with the follow-up of other studies through controlled arteriography at 6–12 months. We rely on the initial consensus agreement to treat stenosis based on the neurological symptoms and not on the degree of stenosis. None of our patients had new ischemic symptoms.

Some of the limitations of our study are the size of the sample and the selection criteria including only patients with stenoses >50% that are refractory to medical therapy. Similarly treated stenoses were both in the anterior and posterior circulation. Other limitation was the lack of long-term arteriographical assessment of stenoses.

In short endovascular therapy of IAS is technically feasible with a short-term high prevalence of adverse events. No recurrence of long-term symptomatology has been detected.

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1. Manager of the study: FA.
2. Study concept: FA, AL, AL, EM and JT.
3. Study design: FA and AL.
4. Data gathering: EM, VVA and FA.
5. Data analysis and interpretation: EM and FA.
6. Statistical treatment: N/A.
7. Bibliographic search: EM and FA.
8. Writing: FA and EM.
9. Critical review and intellectually relevant notes: EM, VVA, AL, AL and JT.
10. Final version approval: FA, EM, VVA, AL, AL and JT.

**Conflicts of interests**

Authors report no relevant conflicts of interests.

**References**

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