Learning curve during percutaneous treatment of carotid lesions

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ABSTRACT

Background
Percutaneous transluminal angioplasty (PTA) of the carotid artery with stent implantation is an effective procedure for the prevention of ischemic stroke but its periprocedural morbimortality is still subject to debate.

Objective
The aim of this study is to report the results of a prospective series of patients treated with PTA.

Methods
This is a descriptive, observational, prospective study using the database of three Hemodynamic centers in Buenos Aires, which included all patients submitted to PTA from January 1998 to December 2010. The results of PTA performed by the same operator were analyzed.

Results
Mean age was 69 years, 58% of the patients were men, 58.8% were smokers, 52% had dyslipidemia, 79.1% were hypertensive, and 28% had diabetes. Prior history of acute myocardial infarction and coronary surgery was present in 19.4 and 11.6% of the patients, respectively. From 1998 to 2004 (initial stage, n=54) 72% of symptomatic patients had indication of revascularization, which was performed without cerebral protection in all cases. During the most recent stage (2004-2010, n=171), only 17.5% of the patients were symptomatic and revascularization was performed systematically with cerebral protection. Similar angiographic success was obtained in both stages (initial 96% vs. recent 97%), whereas clinical success rate was greater in the recent phase (96.1% vs. 87%, p=0.016). There were no cardiac complications. The rate of death or intrahospital stroke was 4%, 4.3% (3/70) in symptomatic and 3.2% (5/155) in asymptomatic patients; moreover, this rate was higher in the initial than in the recent phase (11.1% [6/54] vs. 1.7% [2/171], p=0.0028).

Conclusions
PTA represents an acceptably safe therapeutic alternative to surgical revascularization, providing the procedure is performed by experienced operators.

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Key words > Carotid Stenosis - Carotid Angioplasty - Stroke

Abbreviations >

PTA	Percutaneous transluminal angioplasty	**CP**	Cerebral protection
CE	Carotid endarterectomy		

BACKGROUND
Stroke is the third cause of death in industrialized countries. Only in the United States 795000 cases of stroke are registered annually, presenting high mortality (17.6 %, n = 140.000) and frequently causing permanent physical disability. Extracranial atherosclerotic carotid artery lesions are responsible for at least 20 % of all stroke cases. (2) In the population over 65 years of age, the prevalence of at least 50 % carotid stenosis is 1 – 5 %. Historically, the existence of > 60% carotid stenosis in asymptomatic subjects is associated with a 5% 2-year risk of suffering ipsilat-

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eral stroke, whereas in symptomatic subjects with > 70% stenotic lesion, the 2-year risk is 26%. (4, 5)

In a selected group of patients, carotid revascularization may provide an opportunity to reduce stroke risk. Several studies have shown carotid endarcterectomy (CE) efficacy in the prevention of ischemic stroke in patients with ≥ 50% lesions in symptomatic and with ≥80% lesions in asymptomatic carotid stenosis, with perioperative morbimortality below 6% and 3%, respectively. (4-7) However, there is an increasing number of elderly patients with multiple comorbidities who despite the high surgical risk require revascularization

This has led to the development of other less invasive therapeutic alternatives, such as endovascular techniques. Carotid percutaneous transluminal angioplasty (PTA) and stenting under cerebral protection (CP) is the endovascular technique of choice for the treatment of carotid lesions. (2) Compared to balloon PTA, this technique has reduced re-intervention and distal embolization rate. (2)

In contrast with CE, PTA does not require general anaesthesia or neck incision, thus reducing recovery and hospitalization periods and, consequently the total costs of the intervention. Furthermore, it is not associated with peripheral neurological lesions as CE. Although the role of PTA is currently under revision, it represents a therapeutic option for patients with indication for carotid revascularization and CE contraindication. The purpose of this study is to report the results obtained in a prospective series of patients treated with PTA.

METHODS

This is a descriptive, observational, prospective study using the database of three Hemodynamic centers in Buenos Aires (Sanatorio Güemes, Instituto Médico de Alta Complejidad (IMAC), and Clínica Independencia).

All patients submitted to PTA from January 1998 to November 2010 were included in the study which was performed by the same operator in all cases. A written informed consent was obtained from each patient prior to the procedure. Patients with indication of carotid revascularization (asymptomatic with ≥ 80% stenosis or symptomatic with ≥50% lesion) presenting some of the following high risk variables were considered for PTA: 1) age > 75 years; 2) bilateral carotid disease; 3) contralateral occlusion; 4) ostial common carotid artery lesion or distal internal carotid artery lesion; 5) coronary disease associated with unstable angina; and 6) left ventricular ejection fraction< 35%.

As standard procedure, all patients were referred to clinical neurological evaluation and a carotid Doppler study prior to PTA. In patients with basal neurological deficits or periprocedural neurological symptoms, a control brain imaging study was performed (computed tomography or magnetic resonance imaging). Antiplatelet therapy consisted in periprocedural oral aspirin (325-100 mg given indefinitely) and clopidogrel (loading dose of 300 mg and maintenance dose of 75 mg) or ticlopidine (250 mg every 12 h) for 3 to 6 months. No sedation was used in order to preserve a constant neurological status in the patient. Both arterial pressure and O2 saturation were monitored during the procedure.

Intravenous heparin (70 mg/kg) was administered once the femoral artery was cannulated. In the majority of cases, the puncture site was the femoral artery; only in cases of bovine arch, the radial artery was used. In all cases, angiography of the carotid artery and both vertebral arteries was performed, including intracranial images, to assess collateral circulation in anteroposterior and lateral projections. At the end of the procedure, the same projections were used as comparative method.

In the first cases, the lesion was approached with a telescoping catheter. A 6 Fr JR 3 cm curve guide catheter (Medtronic, Minneapolis, Minnesota, USA) was used through an 8 Fr catheter (Cook Medical Inc., Bloomington, Indiana, USA). They were both advanced through a 0.035" × 150 cm length hydrophilic wire (Glidewire AdvantageTM, Terumo Medical Corp., Tokyo, Japan), leaving the guide catheter just before the carotid bifurcation and removing the JR catheter and the hydrophilic wire to advance the CP device distally to the lesion. Afterwards, depending on the advance of lower profile CP systems, and also of carotid stents, use of the 7 Fr JR 3 cm curve guide catheter was implemented, positioning it in the proximal third of the common carotid artery to advance the CP filter and, according to the lesion, perform direct deployment of the self-expandable carotid stent or predilatation with a 4 mm diameter and 20 cm long balloon catheter followed by stent deployment.

According to the post-implant result, impact was performed with a 5 x 20 mm balloon at 6 atmospheres to retrieve the distal CP filter. It must be emphasized that in our department, CP device implantation started in 2004.

The endpoints were major cerebrovascular events (death, stroke) and transient ischemic attack during hospitalization. Preiprocedural acute myocardial infarction was defined as anginal pain or its anginal equivalent, associated with enzymatic increase, with or without electrocardiographic alterations.

Angiographic success was considered when postprocedural stenosis was less than 30% by visual examination and clinical success as < 30% stenosis without major intrahospital complications (stroke, death, surgery or acute myocardial infarction).

Transient ischemic attack was defined as the neurologic event (hemispheric) with complete recovery within 24 hours of its occurrence. Stroke was defined as every neurological lesion (hemispheric) lasting more than 24 hours. All patients received systematic assessment during hospitalization by a neurologist belonging to the department. Clinical follow-up at 30 days was performed in 95% of the cases, either by phone call or by the patient's physician.

Statistics

Continuous variables are presented as mean ± standard deviation. Categorical variables are expressed as percentages. Categorical variables were compared with the chi-square test or with Fisher's exact test, as appropriate.

Rate of angiographic and clinical success was compared according to the stage of the procedure (initial 1998-2003 vs. recent 2004-2010) and its symptomatic or asymptomatic classification. A p value < 0.05 was considered statistically significant. The statistical package SPSS 11.0 for Windows (SPSS Inc, Chicago, Ill, USA) was used for statistical analysis.

RESULTS

Two hundred and twenty five patients/232 carotid lesions were treated with PTA (Figure 1). Population

demographic characteristics are shown in Table 1. Thirteen percent of the patients were octogenarians, 42% were women and 28% were diabetic. More than a quarter of the patients (26.8%) had coronary disease and 11% had previous carotid revascularization. Thirty one percent of the patients had PTA indication due to ipsilateral neurological symptoms, 72% (29/54) in the initial stage and 17.5% (30/171; $p < 0.001$) in the recent stage.

Procedure characteristics are described in Table 2. Average basal stenosis was 84 ± 11% and 12,4% presented contralateral occlusion. Direct implantation was performed in 38.7% of the cases and postdilatation was frequent (see Table 2).

Angiographic and clinical success rates were 97% and 95.5%, respectively. Even though a similar angiographic success rate was obtained in both stages (initial 96% vs. recent 97%), the rate of clinical success in the recent stage was higher than that obtained in the initial stage (96.1% vs. 87%; $p = 0.016$).

One patient died due to a neurological event (hemorrhagic stroke) associated with the procedure and eight patients suffered stroke (7 ischemic and one hemorrhagic) between 24 and 72 hours after the procedure (Table 3). Seven patients presented cerebral transient ischemic events manifested by dysarthria or brachial hemiparesis, recovering 20-30 minutes after the event; they all evidenced minimal or null intracranial collateral circulation and upon withdrawal of the protection filter this was seen to be occupied by atheromatous material. No other cardiological complications were observed (death or infarction).

The rate of intrahospital death or stroke was 4%, 4.3% (3/70) for symptomatic and 3.2% (5/155) for asymptomatic patients, while this rate was greater in the initial than in the recent stage [11.1% (6/54) vs. 1.7% (2/171); $p = 0.0028$]. No additional events were detected from discharge up to the 30 day follow-up.

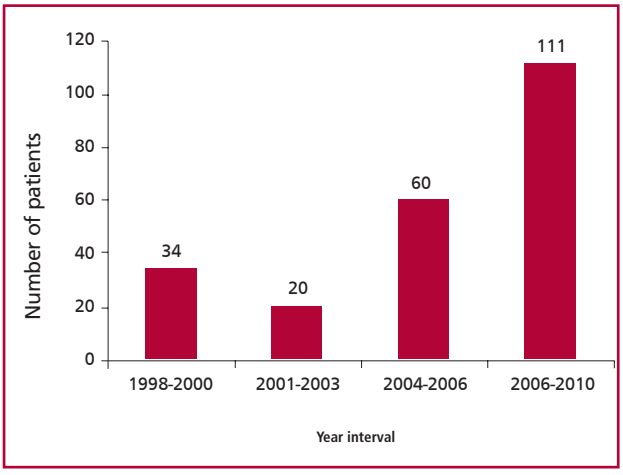

Fig. 1. Basal characteristics (n = 225)

Table 1. Basal characteristics (n = 225)

Age, years	69 ± 10
80 years of age, %	13,1
Men, %	58
Hypertension, %	79,1
Dyslipidemia, %	52
Diabetes, %	28
Smoking, %	50,8
Previos infarction, %	19,4
Previous coronary surgery, %	11,6
Previous carotid endarterectomy, %	9,4
Previous carotid angioplasty, %	6,5

Variables are expressed as mean ± standard deviation or as percentage.

DISCUSSION

In recent years, PTA has improved providing an alternative less invasive therapeutic approach to carotid obstruction. The adoption of this revascularization strategy was especially strengthened after the publication in 2002 of the SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy, n=334) study results. (8) This study compared CE vs. PTA with CP in symptomatic subjects with >50% carotid stenosis or asymptomatic subjects with >80% stenosis. The inclusion criteria required at least one risk factor for CE (age>80, presence of heart failure, severe obstructive pulmonary disease, previous CE with re-stenosis, history of radiation or previous neck surgery, and very distal or proximal carotid lesions). The primary endpoint (stroke, death or infarction at 30 days or death/ipsilateral stroke at one

Table 2. Procedures (patients, n = 225; lesions, n = 232)

Left ICA, %	54,7
% basal stenosis	84 ± 11
Calcification, %	18,7
Ulceration, %	41,8
Contralateral occlusion, %	12,4
Employed Stents, %	
Wallstent	50
Precise	4
Protege	13
Smart	8
Others	25
Direct Stent, %	38,7
Posdilatation, %	71
Distal protection, %*	93,4
Angioguard	2,8
Emboshield	1,1
Epifilter	16,5
Filter Wire EZ	9,1
Spider	68,8
Others	1,7

ICA: Internal carotid artery. *Since 2004.

Table 3. Intrahospital clinical results

	Total (n = 225)
Angiographic success, n (%)	219 (97,3)
Clinical success, n (%)	215 (95,5)
Neurological complications	
TIA, n (%)	7 (3,1)
Ischemic stroke, n (%)	7 (1,8)
Hemorrhagic stroke, n (%)	1 (0,04)
Access site complications	
Death	1 (0,04)

TIA: Transient ischemic attack.

year follow-up) was reached in 12.2% of the cases with PTA and in 20.1% with CE (p = 0.004), while peripheral neurological complication rate was 4.9% and 0% for CE and PTA, respectively. (8) These results led to the approval of PTA by the Food and Drug Administration (FDA) as an alternative treatment for patients at high surgical risk. Several subsequent multicentric studies, as ARCHeR (Acculink for Revascularization of Carotids in High Risk Patient), (9) SECURITY (Registry Study to Evaluate the Neuroshield Bare-Wire Cerebral Protection System and X-Act Stent in patients at high risk for Carotid Endarterectomy), CAPTURE (Carotid Acculink/Accunet Post-Approval Trial to Uncover Unanticipated or Rare Events) (10) and BEACH (Boston Scientific EPI: a carotid stenting trial for high-risk surgical patients) confirmed the safety and efficacy of PTA. (11)

More recently, the CREST study (n = 2502) compared both revascularization techniques in asymptomatic subjects with ≥ 60% stenosis or symptomatic subjects with ≥ 50% stenosis. (12) In this study, prior to participation eligibility, previous PTA training was requested from all operators, and use of only one PC system (Accunet®, Abbott, Santa Rosa, California, United Sates) was mandatory. (12) Although no differences were found in the primary endpoint (death, infarction or stroke at 30 days), the percutaneous treatment presented a higher composite rate of death or stroke at 30 days than the surgical treatment (4.4% vs. 2.3 %; OR 1.90; 95% CI 1.21 to 2.98; p < 0.005), at the expense of a higher stroke rate in the symptomatic group (PTA 5.5% vs. CE 3.2%, p = 0.043). (12) On the other hand, the CE group exhibited higher risk of periprocedural acute myocardial infarction than the PTA group. Moreover, this study and others (13, 14) have reported a high risk of stroke or death in elderly patients submitted to PTA. However, this age group has also been shown to increase CE risk. In a Medicare report of 113300 patients submitted to CE in the United States, patients with ≥85 years presented a threefold higher risk of death than patients below 70 years of age. (15)

At present, there is no evidence of one carotid revascularization technique prevailing over the other in all clinical scenarios, except that both depend on the characteristics of the patient or the lesion.

In our series of patients with carotid stenosis and other important surgical risk factors submitted to PTA, the composite event rate at 30 days (death and/or stroke) was 3.5%, 3.2% in asymptomatic patients and 4.2% in symptomatic patients. These results are favorable compared with those obtained in the CREST study (12) and they are also comparable to those reached in previous studies, such as SAPPHIRE and the global angioplasty registry (16) among others. Likewise, the results attained in our work are similar to the objectives postulated by the American Heart Association/American Stroke Association guidelines: <6% death or stroke risk in the symptomatic group and <3% in the asymptomatic group. (2)

As in the CREST study, our composite rate of periprocedural events was smaller after the exclusion of the initial stage cases, in which 72% of the patients were symptomatic and no CP was used.

Three randomized studies (SPACE, EVA 3S andl ICSS) (17-19) only included symptomatic patients. Unlike SAPPHIRE and CREST, these studies reported a high rate of composite events with PTA, although they generated great controversy due to the presence of methodological errors which probably affected negatively the results of the percutaneous technique. In the SPACE study (n=1200), 73% of the percutaneous procedures were performed without CP. (18) Both techniques reported similar findings (stroke/death at 30 days: 6.84% and 6.34% for PTA and CE, respectively, p= 0.09 for noninferiority) although study enrolment was prematurely discontinued due to lack of funds. (18) On the other hand, in the EVA-3S study (n = 527), the operators had reduced PTA experience (the average PTA of included operators was 1.6 per year), and the study ended prematurely due to the high rate of events in the PTA group. (17) It is necessary to emphasize that in that study CP was not mandatory and 20% of the population did not receive double antiaggregant therapy. Furthermore, PTA without CP was associated with a higher rate of stroke at 30 days (25% vs. 7.9%, p = 0.03) compared to PTA with CP.

There is enough evidence in favor of the complementary use of both proximal (20) and distal (21) CP devices during PTA, and they are essential in symptomatic patients or patients with high risk of embolism. (22)

Several studies have revealed a close relationship between the amount of PTAs perfomed per institution or operator and the result of the procedure. (23-26) In the SAPPHIRE trial, the average operator experience was 64 cases (range 20 – 700) and similarly to surgeons, they had to have an acceptable rate of complications according to the American Heart Association criteria. (8) The need of adequate training and the mandatory use of CP systems are unquestionable in order to warrant acceptable and competitive results with respect to the surgical technique.

Therefore, several factors may have influenced the improvement observed in the rate of events during our recent stage a) a smaller proportion of symptomatic patients, b) greater experience resulting in better selection of patients and improved percutaneous technique, c) technological improvement of percutaneous instruments and CP adoption, d) implementation of advances in pharmacological treatment of carotid disease and secondary prevention. (27, 28)

However, this study has certain limitations that should be pointed out. This is an observational study, based on a relatively small sample, with a reduced follow-up period and without a comparative surgical group. Moreover, there are no available data on cognitive outcome of patients after the procedure.

Due to these limitations, we acknowledge that the present work does not define indisputable therapeutic conducts in patients with such a controversial pathology. However, this is a prospective series of high-risk patients treated with PTA by the same operator with acceptable results, where evident improvement in the outcome is revealed after following a learning curve.

CONCLUSIONS

Findings in the present study suggest that percutaneous treatment of carotid disease is a reasonably safe therapeutic technique, provided it is performed by skilled operators.

RESUMEN

Curva de aprendizaje en el tratamiento percutáneo de las lesiones carotídeas

Introducción
La angioplastia transluminal percutánea (ATP) carotídea con implante de stent es un procedimiento eficaz en la prevención del accidente cerebrovascular (ACV) de tipo isquémico, pero su morbimortalidad periprocedimiento aún es discutida.

Objetivo
Comunicar los resultados de una serie prospectiva de pacientes tratados con ATP.

Material y métodos
Estudio descriptivo, observacional y prospectivo de la base de datos de tres centros de Hemodinamia de la Ciudad de Buenos Aires, en el que se incluyeron todos los pacientes sometidos a ATP carotídea desde enero de 1998 a noviembre de 2010. Se analizaron los resultados de las ATP realizadas por un mismo operador.

Resultados
La edad media fue de 69 años, el 58% de los pacientes eran hombres, el 58,8% tabaquistas, el 52% dislipidémicos, el 79,1% hipertensos y el 28% diabéticos. El 19,4% y el 11,6% tenían historia previa de infarto y cirugía coronaria, respectivamente. Desde 1998 hasta 2004 (etapa inicial, n = 54) hubo un 72% de pacientes sintomáticos con indicación de revascularización; en esta etapa no se utilizó sistema de protección cerebral. En la etapa más contemporánea (2004-2010, n = 171), sólo el 17,5% fueron sintomáticos y el uso de sistema de protección cerebral fue sistemático. Se observó una tasa similar de éxito angiográfico en las dos etapas (inicial 96% vs. contemporánea 97%), en tanto que la tasa de éxito clínico de la etapa contemporánea fue superior a la obtenida en la etapa inicial (96,1% vs. 87%; p = 0,016). No se observaron complicaciones cardiológicas. La tasa de muerte o ACV intrahospitalario fue del 4%, del 4,3% (3/70) en los sintomáticos y del 3,2% (5/155) en los asintomáticos; esta tasa fue mayor en la etapa inicial que en la contemporánea [11,1% (6/54) vs. 1,7% (2/171); p = 0,0028].

Conclusión
La ATP representa una alternativa terapéutica de aceptable seguridad, siempre que sea realizada por operadores experimentados.

Palabras clave > Estenosis carotídea - Angioplastia carotídea - Accidente cerebrovascular

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