

## CAROTID ARTERY IN STENT-RESTENOSIS - A REALITY

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### Abstract

**Introduction.** Restenosis after carotid artery stenting (CAS) is uncommon and usually is asymptomatic. The actual trend is to treat especially symptomatic restenosis.

**Purpose.** The aim of this study was to report data on the incidence and the time of appearance of restenosis after carotid artery stenting and also to report the treatment modalities we used and their outcomes.

**Material and method.** Between 1999 and 2006 in the vascular laboratory of the Heart Institute of Cluj-Napoca were stented 165 symptomatic patients with carotid artery stenoses  $\geq 50\%$ . 173 stents were implanted in this period and the great majority were self-expandable (86,7%). 144 patients were followed systematically. Angiography was performed in hemodynamically significant restenosis ( $\geq 50\%$ ).

**Results.** In this study 144 patients were followed by clinical and doppler examination. Rate of restenosis was 4,16%. It was treated successfully by angioplasty and or stenting. We encountered 1 major intraprocedural complication: acute stent thrombosis that was managed successfully by administration of thrombolytic (intracarotid). A DES was delivered in one patient for re-restenosis.

**Conclusions.** After carotid artery stenting, restenosis appeared in 4,16% of cases. Half of the cases were symptomatic. It was treated safely with percutaneous intervention with minimal complications. Because of the symptoms that appeared in half of the cases this entity deserve special attention; in some cases it could be not a benign process. A drug-eluted stent implanted for re-restenosis has good short and long term results being promise for other cases with CAS restenosis and high-risk surgical conditions and extensive vascular disease.

**Keywords:** carotid artery, carotid stenosis, angioplasty, stent, restenosis.

## RESTENOZA ÎN STENTUL CAROTIDIAN – O REALITATE

### Rezumat

**Introducere.** Restenoza în stentul carotidian nu este frecvent întâlnită și este de obicei asimptomatică. Tendința actuală este de a trata în special restenoza simptomatică.

**Obiective.** Scopul acestui studiu a fost de a raporta date asupra incidenței restenozei în stentul carotidian și asupra timpului de apariție a acesteia, precum și modalitățile de tratament pe care le-am folosit.

**Material și metodă.** Între 1999-2006, în laboratorul de cardiologie intervențională al Institutului Inimii au fost efectuate proceduri de stentare carotidiană la 165 de pacienți. Toți pacienții au fost simptomatici și au avut stenoze ale carotidei interne  $\geq 50\%$ . În decursul acestor proceduri s-au implantat 173 de stenturi și majoritatea au fost auto-expandabile (86,7%). 144 de pacienți au fost urmăriți sistematic. Cei cărora li s-a detectat restenoze semnificative hemodinamice ( $\geq 50\%$ ) li s-a efectuat angiografie.

**Rezultate.** În acest studiu 144 de pacienți au fost urmăriți clinic și ecografic. Rata de restenoză a fost de 4,16%. Restenoza a fost tratată cu succes prin angioplastie și/sau stentare. Am înregistrat o singură complicație majoră: tromboza acută de stent, ce a fost tratată cu succes prin administrarea de trombolitic intracarotidian. Unui

*pacient i s-a implantat un stent farmacologic activ pentru re-restenoză.*

**Concluzii.** Restenoza după stentarea carotidiană a apărut în 4,16% din cazuri. Jumătate dintre pacienții cu restenoză au fost simptomatici. Restenoza a fost tratată cu succes prin proceduri invazive percutane cu complicații minime. Deoarece simptomele au apărut la jumătate din pacienții cu restenoză, considerăm că această entitate merită o atenție deosebită; în anumite cazuri ar putea să nu fie un proces benign. Un stent farmacologic activ implantat pentru re-restenoză a avut rezultate pe termen scurt și lung foarte bune. Stenturile farmacologic active ar putea constitui soluția în cazurile de restenoză carotidiană la pacienții cu boală extensivă vasculară și cu risc înalt chirurgical.

**Cuvinte cheie:** arteră carotidă, stenoza carotidiană, angioplastie, stent, restenoză.

## Introduction

Carotid artery stenting (CAS) is an acceptable and less invasive alternative to carotidendarterectomy (CEA) approved by FDA in symptomatic patients considered high-risk for surgery where it is the treatment of choice with results equal to surgery when performed by experienced operators.

Because the population of patients who have been treated with stent placement is growing, we encounter more frequently in-stent restenosis. According to literature restenosis is reported in 2-8,9% of cases [1,2]. In the majority of cases it is asymptomatic

Recent studies suggest as a predictor of future restenosis technical factors such as minimal lumen diameter obtained immediately after the invasive procedure [3]. The actual trend is to treat especially symptomatic restenosis.

At this moment there is no agreement about the optimal treatment of the carotid artery stent restenosis: surgery versus endovascular treatment.

## Purpose

The aim of this study was to report data on the incidence and the time of appearance of restenosis after carotid artery stenting and also to report the treatment modalities we used and their outcomes.

## Material and method

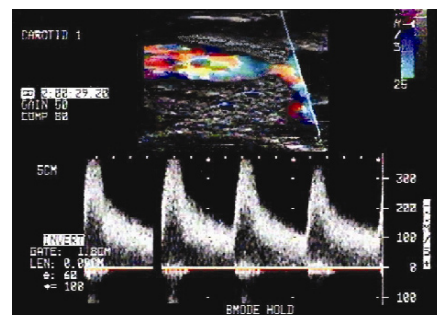
We reviewed the data on the 165 consecutive patients who underwent CAS (173 stents) from 1999 to 2006 in the vascular laboratory of the 'Heart Institute' in Cluj-Napoca, Romania. All patients had symptomatic carotid artery stenosis with a severity of at least 50% (defined using NASCET criteria). All of them had a neurological exam and a baseline CT. 173 stents were implanted in this period and the great majority were self-expandable (86,7%). Only at the beginning of the studied period, balloon-expandable stents were used (13,3%).

Patients were followed by clinical examination and

by sonography every 6 months in the first year and yearly thereafter. This protocol of surveillance was followed by 83% of patients, (144 patients). CAS patients with suspected in stent restenosis  $\geq 50\%$  by US were referred for angiography.

## Duplex ultrasound examination

Ecographic examination was performed using a HP Sonos 5500 ecographic machine with a transducer of 7,5 MHz. Velocities were measured in the stented carotid arteries (proximal, middle and distal) and in the terminal common carotid artery (CCA) respectively. Duplex-ultrasound examination of the carotid arteries is the simplest method routinely used to monitor the patency of the carotid stents and the eventual restenosis. The evaluation is based on the measurement of the flow velocities in the native common carotid artery and intrastent respectively. The criteria for defining a severe stenosis differ from those encountered in native carotid arteries because stent deployment result in changes in vessel wall compliance and blood flow (location for Fig. 1A).



**Fig. 1A – ISR - Doppler criteria**

Peak systolic velocity (PSV) was measured intrastent and in CCA and a ratio of them was obtained. The criteria of Yung-Wei Chi were used to quantify the severity of ISR: PSV of 240cm/sec and ICA/CCA=2.45 for a stenosis of  $\geq 50\%$  and PSV>450cm/sec and ICA/CCA = 4.5 for a restenosis of  $\geq 70\%$  [4].

## Angiographic analysis

Invasive angiography was performed in patients with ISR of  $\geq 50\%$  as detected by US. Anteroposterior, oblique and lateral views were obtained. The severity of

restenosis was established using the NASCET criteria. The narrowest luminal diameter was compared to the nearest normal distal segment of the normal ICA and was expressed as a percentage (location for Fig. 1B).



**Fig. 1B** – ISR - angiographic criteria.

### Results

In this study 144 patients from a total of 165 were followed after CAS (83%). 40 patients of those 144 followed the study surveillance protocol at irregular intervals.

Six patients were detected by US with ISR and confirmed angiographically. One patient had a 50% ISR and, because he was asymptomatic, he is followed clinically and by duplex echography at regular intervals. The patients' ages were between 51 and 80 years. Four were men and two were women. The time to carotid restenosis was 6 months in a patient, (followed by a second restenosis after an initial angioplasty for the first restenosis), 1 year in another one, 17 months, 18 months and 3 years in the others two (the last 2 patients were followed for the first time after the CAS at 3 years because of the their poor cooperation).

Three patients were symptomatic, the other three were asymptomatic. All patients with restenosis had high-risk criteria for carotid surgery. None patient had a prior carotid surgery or a history of neck irradiation.

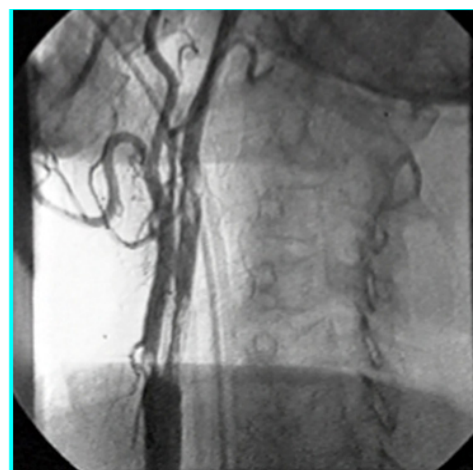
The restenosed stents were: 3 self-expandable, 1 bare metal stent and 2 balloon-expandable stents, respectively.

It is worthfull to mention that all three symptomatic patients were initially treated for in stent restenosis by angioplasty alone. All of them were high-risk candidates for surgery, with extensive vascular disease. After PTA, all of them remained with a residual stenosis 15%, 15% and 20% respectively. All three of them presented with re-restenosis.

One re-restenosis manifested as a TIA, the other two were asymptomatic. The CT scans were negative in all three cases but we did not have the possibility to perform a diffusion-weight MRI with a greater sensibility.

The treatment of restenosis consisted in angioplasty (PTA) and self-expandable stent deployment in 3 patients, and angioplasty alone in 3 patients; a DES was used for the re-restenosis in one patient. The other 2 re-restenosis are under strict surveillance at this time. All of them had

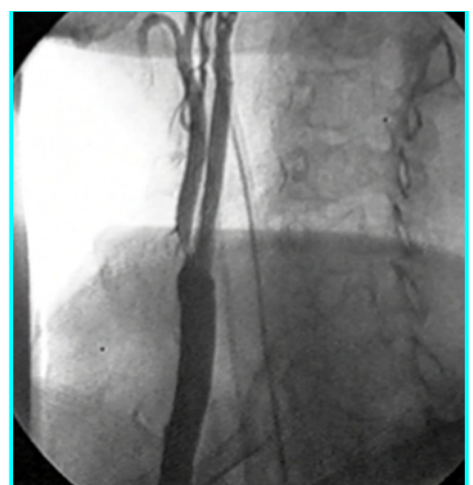
a permanent medication with aspirin (150 mg/day) and ticlopidine or clopidogrel for one month. In one case intraprocedural complications appeared (stent thrombosis promptly resolved by intra-arterial thrombolysis) (location for Fig. 2A, 2B, 2C).



**Fig. 2A** – Intrastent thrombosis.



**Fig. 2B** – Intrastent trombolysis.



**Fig. 2C** – Final aspect.



# Discussions

Carotid artery stenting is performed with increasing frequency. The long term patency of the stents is not assessed by large clinical trials. It is very important to established the consequences of a restenosis on the cerebral circulation and the risk for future stroke. Symptomatic ISR in the carotid artery has a low incidence but, with possible serious complication. Symptoms can mimic an embolic stroke like in a native stenoses or cognitive deficits as demonstrated by improvement of cognitive function after restoration of blood flow through carotid artery [5].

Mechanisms responsible for ISR are neointimal hyperplasia in the majority of cases and thrombus, respectively (20%). Even the neointimal hyperplasia is considered a benign condition, thrombus may release micro emboli in the cerebral circulation [6], which was demonstrated by filter capture of thrombotic fragments during protected balloon dilation [7]; in our experience in one case of restenosis manifested clinically as transient ischaemic attack (TIA) we had filter obstruction during the interventional procedure. In stent restenosis can transform into occlusion.

Two types of stents are used for the carotids: balloon-expandable stents with the possible danger of stent crushing and self-expanding stents.

Carotid IVUS studies demonstrated that intracarotid auto-expandable stents continue to enlarge after their deployment reaching an area at 6 months 25-33% greater than the initial one but this process is reversed by the 30-40% neointimal hyperplasia so that the lumen loss is comparable with that in balloon-expandable stents [3].

In this retrospective analysis we find an incidence of ISR of 4,16% that compares with other studies [8]. In contrast with other analysis, in the population studied, previous CEA and irradiation were not found to be risk factors for restenosis [9]. Concordant with other studies ISR appeared predominantly at old ages [10], in males with diabetes, hypertension and dyslipidemia with extensive

vascular disease.

The optimal treatment for ISR was not defined yet. The surgical treatment is technically difficult but possible with stent extraction and carotid reconstruction by a graft interposition. Raithel published the largest series of 8 patients, all of whom underwent surgical exploration for recurrent ISR (>80%) following failed secondary percutaneous interventions (balloon angioplasty). Standard CEA with stent removal was performed. The authors frequently encountered periarterial inflammatory scarring and difficulty in extracting the stent.

In this study the ISR treatment consisted of angioplasty ± stenting. The three symptomatic cases appeared after an initial balloon angioplasty with residual stenosis (15% in two cases and 20% in another one.). We have to mention that in one of this patient a DES was deployed in ICA for a re-restenosis [11]. The patient is followed for five years without signs of restenosis (location for Fig. 3A, 3B).

At this time there are no trials to demonstrate the safety of DES in the carotid artery territory, but there are a few small studies that demonstrated the DES delivery in the cerebral circulation is feasible with good short and intermediate-term results with no toxic effects on the cerebral circulation [12]. Future randomised trials could demonstrate that DES could be a real option for ISR in the carotid arteries territory in selected cases in which actions for repeated restenosis could be more dangerous than DES itself. (the risk of late thrombosis does exist especially when the clopidogrel treatment is interrupted).

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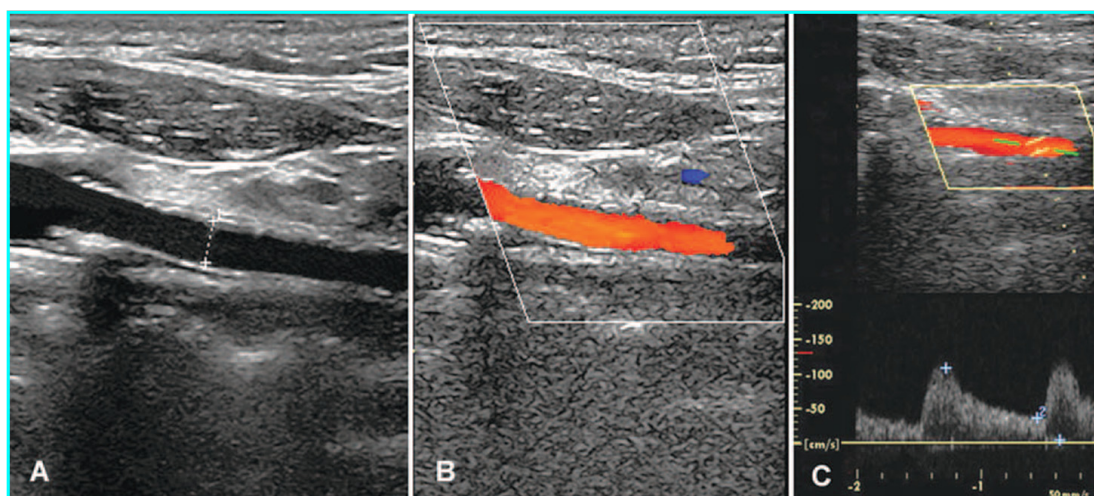


Fig. 3 A,B,C – DES 5 years after insertion – Doppler aspect.

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