ORIGINAL ARTICLE

Carotid artery stenting: Clinical and procedural implications for near-occlusion stenosis

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Stent; Revascularisation; Cerebrovascular circulation; Cerebral infarction

Abstract
Introduction and objectives: The advisability of implanting a stent in carotid near-occlusion stenosis is a controversial topic. We have assessed procedural and clinical implications of stent implantation for carotid artery disease with near occlusion.

Methods: We included 205 patients who underwent carotid artery revascularisation with a stent. The group of patients with near-occlusion stenosis (n = 54) was compared to the rest of the population (n = 151).

Results: No differences were found between groups for age, sex, and the percentage of symptomatic patients (three-quarters of the population). Carotid stent revascularisation for near-occlusion stenosis presented a high procedural success rate (96%) similar to that of revascularisation processes for other lesions (98%). Stenting in cases of near-occlusion stenosis required increased use of proximal protection (54% vs. 20.5%, P < 0.001) and predilation (33% vs. 17%, P = 0.01). The process to repair near-occlusion stenosis causes increased detachment of plaque, as shown by higher percentages of macroscopic plaque captured by protection devices (18.5% vs. 7%, P = 0.01) and of perioperative ischaemic brain lesions (47% vs 31%, P = 0.07). At 30 days of follow-up, the tendency towards adverse neurological events (death, major and minor stroke) was higher in the near-occlusion group (9.2% vs. 3.2%, P = 0.08).

Conclusions: Stent revascularisation for near-occlusion carotid stenosis has a high procedural success rate; however, its higher plaque load was responsible for the increased rate of ischaemic brain lesions and adverse neurovascular events at 30 days post-procedure.

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Introduction

Cerebrovascular diseases have a high incidence rate in Spain (166.9 strokes and 36.7 transient ischaemic events per 100,000 inhabitants per year). They are the leading cause of death among Spanish women, and the second most common among men. 1 Approximately a third of all strokes are due to extracranial carotid artery disease. 2 Characteristics of the carotid plaque (severity of the obstruction, presence of an ulcer or thrombus, etc.), plus the extent of its symptoms, constitute the variables most closely related to the risk of having a cerebrovascular accident. 3,4

Carotid stenosis near-occlusion (CSNO) still presents a treatment dilemma. 5 On the one hand, critical carotid lesions may exhaust the intracranial vasoregulatory capacity, and this has been associated with an increased risk of cerebrovascular events. 6 Nevertheless, the main mechanism of stroke due to carotid artery disease is embolus of atherothrombotic material that breaks off of plaque. The greater the severity of the obstruction, the greater the risk of embolism; however, risk is lower in near-occlusion stenosis because there is less blood flow to the brain. 7

The purpose of this study is to investigate the clinical and procedural implications of treating near occlusion of the carotid artery with stent compared to other carotid conditions treated with percutaneous revascularisation.

Methods

This descriptive single-centre study included, in consecutive order, patients who underwent carotid stenting between January 2008 and March 2012 at Hospital Virgen Macarena (Seville). We compared 2 populations, those with and without near occlusion of the carotid artery.

A multidisciplinary neurovascular team made up of neurologists, radiologists, and interventional cardiologists was responsible for carotid artery stenting in our hospital. The neurologist’s role was to indicate the procedure, monitor the patient during the intervention, and review his or her neurological status at 24 hours and at 30 days post-surgery. The carotid intervention was performed by 2 interventional cardiologists (R.R.S. and C.C.) who had completed structured training in this procedure (monitored theoretical training, viewing procedures in a high-volume centre, and rehearsing skills using a simulator). They were assisted in the first 5 cases by an expert interventional radiologist.

We assessed the success rate for the procedure (implantation of a stent in the internal carotid with no neurovascular events — minor stroke, major stroke, or death) in the first 24 hours and the cumulative rate of neurovascular events in 30 days. We also recorded presence of infarct shown by MR studies in the 10 days after the procedure.

Quantitative analysis of carotid lesions. Definition of near occlusion of the carotid artery

Carotid stenosis and the result of the revascularisation procedures were measured using Siemens Artis zee software (CAAS II, Pie Medical, The Netherlands). Stenosis severity was not measured according to NASCET criteria (the ratio of the minimum diameter of the stenosis to the reference value for the internal carotid). This is because in the cases...
of near-occlusion, the internal carotid artery frequently displays loss of calibre due to the decreased flow. For that reason, we have opted to use the diameter of the common carotid artery prior to the development of stenosis as the reference value.

CSNO has been defined in early studies by applying a series of qualitative criteria\(^3\): decrease in the calibre of the internal carotid artery with respect to the common or internal contralateral artery, slower contrast transport in the internal carotid than in the external carotid, and/or evidence of intracranial collateral pathways. These criteria, which are indirect signs of the severity of plaque obstruction in the carotid, cannot be applied to the entire population with CSNO. For example, lack of continuity in the circle of Willis limits the presence of collateral pathways, while severe disease or contralateral carotid occlusion is an obstacle to evaluating collateral pathways and comparing flow and calibre between the two internal carotid arteries. On the other hand, the lesion may compromise the origin of the external carotid artery, and therefore its filling velocity. For this reason, we have added critical severity of obstruction (minimum luminal diameter less than 1 mm) to the listed qualitative criteria (Fig. 1).

Collateral intracranial circulation ipsilateral to the stenotic area was classified on a 3-point scale: absent, discrete (only filling from the anterior cerebral artery), and excellent (filling from the anterior and middle cerebral arteries ipsilateral to the stenotic lesion).

**Revascularisation procedure for carotid artery with stent implantation**

Our unit indications carotid revascularisation procedures based on the following criteria\(^4\): symptomatic patients (neurological signs in the preceding 6 months) with significant carotid stenosis (>50%) and asymptomatic patients with carotid stenosis >60% and occlusion of the contralateral carotid artery.

The only diagnostic test which patients underwent prior to the procedure was carotid Doppler ultrasonography to measure severity of the obstruction and plaque characteristics.

The procedure was performed using an embolic protection device as a routine safeguard. Our group used distal embolic filters (Angioguard, Cordis, USA) and proximal protection devices (MoMa, Medtronic, Italy) (Fig. 2). Protection was selected according to the lead interventionist’s clinical judgement and depending on a series of factors: plaque severity and characteristics, vessel tortuosity, and presence of significant disease in the contralateral carotid.

Pre-dilatation was only performed when the stent would not pass through the stenosis, regardless of the embolic protection device employed. However, all patients underwent post-dilatation using a 5 mm balloon. We used different types of open-cell stents (Protege, eV3; Acculink, Abbott; Precise, Cordis, USA) and mixed-design stents (Cristallo, Medtronic, Italy) indiscriminately.

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**Figure 1**  (A) Carotid artery near-occlusion meeting all qualitative criteria for that definition: internal carotid artery (arrow) with a diameter smaller than that of the external carotid (arrowhead); distal opacification in the territory of the internal carotid, which is smaller than the external carotid (*); compensation by collateral intracranial circulation (B). (C) Result after placement of Cristallo stent (Invatec-Medtronic). The inflated distal balloon (#) of the MoMa device (Invatec-Medtronic) can be seen at the origin of the external carotid artery.
After an initial phase, we modified the intervention method in 2 ways. First, we suppressed routine administration of 1 mg atropine prior to post-dilatation in order to achieve better control over arterial pressure during the phase just after the intervention. Additionally, we monitored patients for the 6 hours following revascularisation, with particular attention to arterial pressure. Doses of antithrombotic agents were also changed. In the early phase of the study, patients were on dual antiplatelet treatment. During the procedure, they received 100 U of heparin sodium/kg body weight, plus a set dose of 300 mg clopidogrel after placement of the stent. In 2010, we decided to change the anti-thrombotic treatment so that the patient would receive 50 U heparin sodium/kg body weight with no extra doses of clopidogrel. During the first month, the patient remained in treatment with dual antiplatelet drugs.

**Statistical analysis**

After being entered in an Excel spreadsheet (Microsoft Office 2007, USA), data were analysed using SPSS statistical software, version 20.0. Continuous variables were described as means ± standard deviations; categorical variables were expressed as numerical values and percentages. We compared variables from 2 independent samples (group of patients with CSNO and the group of other patients with revascularisation procedures). The t-test was used for continuous variables and the chi-square test was used for categorical variables.

**Results**

These 4 years of activity have seen 205 carotid revascularisation procedures in our unit; 54 were performed to treat CSNO (26%), while the remaining 151 treated cases were significant but not near-occlusive lesions (non-CSNO, 74%).

**Clinical characteristics**

Baseline clinical characteristics for both groups are listed in Table 1. Both populations presented high and comparable percentages of symptomatic patients, who made up three-quarters of the total. There were no significant differences in cardiovascular risk factors with regard to smoking habits, arterial hypertension, and diabetes. Nevertheless, patients with CSNO lesions had higher dyslipidaemia rates (85% vs 69%, P = 0.02). The 2 groups also differed with regard to non-carotid cardiovascular disease (coronary or peripheral vessel disease). Patients in the non-CSNO group showed a

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**Periprocedural assessment of ischaemic brain lesions**

Doctors ordered brain MRI studies (sagittal T1-weighted, axial T2-weighted, diffusion-weighted with ADC mapping, and coronal FLAIR images) for all patients in the 10 days following the procedure, except where contraindicated. In the end, 137 patients were evaluated (67% of the population); the main given for lack of an evaluation was logistical difficulty arranging the evaluation in the allotted time frame. MRI studies were completed using a Magnetom Symphony 1.5 T unit (Siemens, Germany) with diffusion-weighted sequences. Areas that were hyperintense in diffusion-weighted sequences and hypointense in ADC maps (Fig. 3) were considered recent-onset ischaemic lesions.
significantly higher frequency of non-carotid cardiovascular disease than the others (63% vs 48%, P=0.05).

Angiographic and procedural data

Table 2 summarises angiographic findings and the characteristics of the stent placement process. In the CSNO group, the minimum luminal diameter was 0.5 ± 0.3 mm. In this group, in addition to severity of the obstruction (minimum luminal diameter < 1 mm), we evaluated the presence and quality of the collateral intracranial circulation. In 38 patients (70% of the CSNO group), the CSNO lesion was accompanied by collateral intracranial circulation which was discrete in 14 patients (filling from the anterior cerebral artery only) and excellent in the other 24 (involvement by the anterior and medial cerebral arteries).

There were differences in the revascularisation procedures between the 2 groups. A larger percentage of the near-occlusion cases required pre-dilatation (33% vs 17%, P=0.01), although percentages remained low overall. The most noteworthy procedural differences had to do with the method of protection: use of a proximal protection device (MoMa) was significantly more frequent for near-occlusion cases than for other cases (54% vs 20.5%, P<0.001). We should point out that the intolerance rate for MoMa was higher in the non-CSNO group (5.5% vs 32%, P=0.04). Lastly, there were also significant differences between groups regarding capture of embolic material. More macroscopic material was present in revascularisation cases with CSNO lesions (18.5% vs 7%, P=0.01) (Fig. 4).

Carotid stent revascularisation according to stenosis severity: clinical implications

The success rate for procedures for CSNO cases was 96%. The procedure failed in 2 patients due to the appearance of a minor neurological deficit (1 case of amaurosis fugax, 1 case of mild upper limb paresis); both cases resolved completely. Success rate in the non-CSNO group was 98%, with 3 procedures being unsuccessful. In one case, the patient suffered a major stroke due to embolisation of material in the middle cerebral artery; the material was successfully extracted during the same procedure by thrombectomy with a Solitaire stent (eV3, USA). In the other 2 cases, patients

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline clinical characteristics.</th>
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<tr>
<td></td>
<td>CSNO group (n = 54)</td>
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<tr>
<td>Age (years)</td>
<td>67 ± 11</td>
</tr>
<tr>
<td>Octogenarians (%)</td>
<td>8 (15)</td>
</tr>
<tr>
<td>Males (%)</td>
<td>45 (83)</td>
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<tr>
<td>Smokers (%)</td>
<td>33 (61)</td>
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<tr>
<td>Arterial hypertension (%)</td>
<td>39 (72)</td>
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<tr>
<td>Dyslipidaemia (%)</td>
<td>46 (85)</td>
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<tr>
<td>Diabetes (%)</td>
<td>22 (41)</td>
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<tr>
<td>Other cardiovascular disease (%)</td>
<td>26 (48)</td>
</tr>
<tr>
<td>Symptomatic (%)</td>
<td>40 (74)</td>
</tr>
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</table>

±: mean ± SD.
suffered minor neurological disorders, which were transient in both cases.

The groups had identical percentages of cases with brain MRI studies (36 CSNO cases and 101 non-CSNO cases; 67% in both groups). Periprocedural ischaemic lesions were present in 47% of the patients with near-occlusive stenosis (88% silent); 31% of the non-CSNO patients had ischaemic lesions revealed by MR studies (90% silent) (P = 0.07).

Three intracranial haemorrhages occurred in the first month after surgery, and they were fatal in patients with CSNO (mortality rate of 5.5%). In the other patient group, there was only 1 mortality due to intracranial haemorrhage in the month following surgery (0.6%). Hyperperfusion syndrome after revascularisation may have been the cause of the intracranial haemorrhage. All these cases occurred in symptomatic patients, 3 of whom had suffered a recent infarct in the territory of the ipsilateral middle cerebral artery.

The frequency of all neurological events within 1 month of the procedure was 9.2% in the CSNO group (3 deaths and 2 minor strokes) and 3.2% in the non-CSNO group (1 death, 1 major stroke, and 3 minor strokes; 10 days after the procedure, a patient experienced thrombosis of the central retinal artery). This reflects a tendency towards increased event frequency in the first group (P = 0.08).

**Discussion**

This study compiles experiences with treating near-occlusive carotid stenosis from a neurovascular team including neurologists, radiologists, and interventional cardiologists.

Revascularising CSNO lesions by stent placement was highly successful as a procedure, but it also entailed an increased number of neurological complications in the first month compared to revascularisation procedures for less severe stenosis. The larger plaque substrate in near-occlusive lesions resulted in a higher rate of intracranial ischaemic lesions after surgery. In addition, patients were more prone to intracranial bleeding due to hyperperfusion syndrome.

**Population with carotid stenosis near-occlusion**

CSNO cases made up 26% of our population, which shows that the condition is common in daily practice. According to the literature, the frequency of CSNO lesions requiring revascularisation ranges from 14% to 29%,<sup>6,10</sup> and the meta-analysis of the NASCET and ESCT studies showed a mean of 21.5%.<sup>7</sup>

The question of whether CSNO should be treated remains unanswered at present.<sup>3—8</sup> The risk of suffering a neurological event due to carotid disease depends largely on the
degree of obstruction. Plaques with the most risk of caus-
ing stroke are those involved in 90% to 99% stenosis. In this
group, cases with near-occlusive plaque (95%–99%) present
a lower risk of stroke than cases with stenosis in the 90%
to 94% range. This occurs because most strokes are caused
by embolisation of thrombotic material, not by low blood
flow caused by the obstruction. To a certain extent, near-
occlusion may ‘protect’ a patient from embolism and stroke.
However, CSNO lesions evolve towards carotid occlusion, and
if circumstances are favourable, the impact of this occlusion
on the patient’s cognitive abilities may be underestimated.

Angiography and treatment approach for carotid
stenosis near-occlusion

The NASCET criteria for measuring carotid stenosis under-
estimate the degree of severity of CSNO lesions since the
diameter of the internal carotid artery decreases as the
degree of obstruction increases. With this in mind, other
authors have identified CSNO based on exclusively qualita-
tive angiography criteria.7 We used the same criteria, with
the addition of the quantitative measurement of a minimum
luminal diameter of less than 1 mm. Indirect signs of the
severity of the obstruction may not manifest clearly for a
number of reasons (generally because of occlusion of the
contralateral internal carotid artery).

Whether embolic protection devices should be deployed
during stent revascularisation remains a controversial topic,
and it has a very low recommendation level according to
recent European clinical practice guidelines.8 Nevertheless,
our group used distal or proximal protection devices dur-
ing all procedures. Larger amounts of plaque, and possibly
more unstable plaque composition, are factors explaining
why the CSNO group had a higher rate of macroscopic mat-
erial extracted by the embolic protection devices than the
other group (18.5% vs 7%), as well as a higher frequency
of cerebral ischaemia (47% vs 31%). Fortunately, this high
percentage of ischaemic brain lesions was not correlated
to clinical symptoms, except in 2 patients, each of whom
suffered a minor stroke.

Stent revascularisation in near-occlusive stenosis

The success rate for the stent revascularisation procedure
for CSNO was high and comparable to rates for less severe
lesions (96% vs 98%). This tendency has been described in
prior studies. Despite the high success rate, 3 patients with
near-occlusive stenosis (5.5% of the population) presented
symptoms of intracranial haemorrhage within a month of
the procedure, and all died. Where no other factors are
present, intracranial haemorrhage is due to hyperperfusion
syndrome as a result of breaking the blood–brain barrier
when revascularising a severely stenotic artery whose distal
arteriolar bed has an exhausted vasodilator reserve. Fac-
tors predisposing an individual to hyperperfusion syndrome
after carotid revascularisation include treatment of critical
lesions, severe contralateral occlusion or stenosis, peri-
procedural hypertension,9 and excessive anticoagulant use.10
In our population, 4 patients developed hyperperfusion syn-
drome with intracranial haemorrhage resulting in death.
Three were in the CSNO group (including 2 patients with
no collateral intracranial circulation), and 1 in the other
patient group. All deaths occurred in the first 2 years of our
experience with the procedure (2008 and 2009). Since ant-
ithrombotic treatment was modified to reduce anticoagulant
dosage and eliminate the loading dose of clopidogrel, and
since doctors began prioritising control over arterial pres-
sure during and after procedures, no other hyperperfusion
events have occurred.

The cumulative 30-day fatality and stroke rate in the
CSNO group was 9.2%, compared to 3.2% in the rest of
the patients. This difference approached statistical signifi-
cance. The higher rate of events in the CSNO group is due to
deaths from intracranial haemorrhage. The 2 ischaemic strokes
in this group were minor events and patients had recovered
completely 30 days later.

Limitations

This study has numerous limitations. First, its definition
of near-occlusion stenosis contains an additional, and not yet
validated, quantitative angiography measurement. If this
were not the case, a third of the patients in the near-
occlusion group, precisely those at the most risk for severe
clinical complications from a revascularisation procedure,
would not have been included in the group. Secondly, we did
not analyse lesions according to their symptomatic repercus-
sions, although there was a similar, and predominant,
percentage of patients with symptoms in both groups. Lastly,
clinical follow-up ended at 30 days, and more long-term eval-
uations will be needed.

Conclusion

Our experience shows that stent revascularisation for CSNO
lesions is an effective procedure, but its 30-day morbidity
and mortality rates are higher than those for the treatment
of less severe stenosis. On the one hand, stent implantation
results in more plaque material being loosened. Despite the
use of protective devices, this will result in a higher per-
centage of cerebral ischaemia. On the other hand, we find
a higher rate of neurological events, mainly death due to
intracranial haemorrhage, within 1 month of the revascular-
isation procedure. For these reasons, stent revascularisation
for CSNO cases should be performed following an analysis of
the patient’s individual clinical and angiographic character-
istics. Extreme caution must be used during the procedure
(adjusting antithrombotic drug doses, using embolic protec-
tion devices, and monitoring blood pressure values).

Conflicts of interest

The authors have no conflicts of interest to declare.

References

representación del Proyecto Ictus del Grupo de Estudio de Enfer-
medades Cerebrovasculares de la SEN. Incidencia del ictus en