Thirty-Day Outcomes of Direct Carotid Artery Stenting With Cerebral Protection in High-Risk Patients

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Background  Implantation of a carotid artery stent after predilation is a standard approach in the endovascular treatment of carotid artery stenoses. Stenting without predilation may be an alternative approach in a certain subset of patients. The present prospective, single-center registry was designed to evaluate the feasibility and safety of direct carotid artery stenting (DCAS) in high-risk patients.

Methods and Results  Symptomatic patients with stenosis >50% and asymptomatic patients with stenosis >70% were eligible for enrolment. Criteria for high-risk patients included: need or history of open heart surgery, history of myocardial infarction, multivessel coronary artery disease, left ventricular dysfunction (ejection fraction ≤40%), severe pulmonary or renal disease, significant contralateral carotid disease, previous endarterectomy, and age ≥80 years. All procedures were performed using a filter protection device. Patients underwent complete clinical examination before and after DCAS and at 30-day follow-up. A total of 83 consecutive patients (45 males, 68±9 years, 33% symptomatic) underwent 100 procedures and 103 stents were deployed successfully. The technical success rate of stenting was 100%. Predilation of carotid stenosis was necessary in 1 (1%) procedure. Carotid-artery stenoses before and after DCAS were 80±9% and 7±9%, respectively. The median fluoroscopic time for DCAS was 7 min. The overall rate of in-hospital major adverse cerebrovascular events (death, stroke, myocardial infarction) was 5% (2 minor strokes, 3 transient attacks). There was 1 (1%) minor stroke within the 30-day follow-up.

Conclusion  DCAS is feasible and can be performed with an acceptable risk in high-risk patients. (Circ J 2007; 71: 1468–1472)

Key Words:  Carotid; Peripheral intervention; Stent

Sev--eral trials have shown that carotid endarterectomy is superior to medical treatment alone for the prevention of stroke in patients with significant carotid artery stenosis.1–5 The SAPPHIRE trial has established carotid artery stenting (CAS) in high-surgical-risk patients as an effective alternative to carotid endarterectomy.6 CAS after previous balloon dilation has been shown to be a safe, effective, and durable method of treatment for carotid artery disease.2

We started carotid artery interventions in 1998 and with the exception of the treatment of in-stent restenosis, every carotid intervention implies elective stent implantation. From an initial strategy of predilation followed by stent implantation, we now perform direct carotid artery stenting (DCAS) for the vast majority of lesions.

The present prospective, single-center registry was designed to evaluate the feasibility and safety of DCAS with distal protection devices in consecutive patients who were scheduled for endovascular treatment of significant carotid stenoses. A safety and feasibility evaluation of the aggressive approach in indication to endovascular therapy (and only exceptional indication to carotid endarterectomy) was another aim of our study.

Table 1  Baseline Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Age, years (range)</th>
<th>68±9 (46–84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥80 years (%)</td>
<td>10/12</td>
</tr>
<tr>
<td>Gender (male; %)</td>
<td>45/54</td>
</tr>
<tr>
<td>Symptoms (%)</td>
<td>27/33</td>
</tr>
<tr>
<td>Prior endarterectomy (%)</td>
<td>2/2</td>
</tr>
<tr>
<td>History of myocardial infarction (%)</td>
<td>32/39</td>
</tr>
<tr>
<td>Previous coronary artery bypass grafting (%)</td>
<td>19/23</td>
</tr>
<tr>
<td>Previous coronary artery intervention (%)</td>
<td>32/39</td>
</tr>
<tr>
<td>Known multivessel coronary artery disease (%)</td>
<td>57/69</td>
</tr>
<tr>
<td>Left ventricular dysfunction (%)</td>
<td>14/17</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>22/27</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>76/92</td>
</tr>
<tr>
<td>Hypercholesterolemia &gt;5 mmol/L (%)</td>
<td>12/14</td>
</tr>
<tr>
<td>Hypertriglyceridemia &gt;2 mmol/L (%)</td>
<td>23/28</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>39/47</td>
</tr>
<tr>
<td>Renal insufficiency (%)</td>
<td>16/19</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (%)</td>
<td>18/22</td>
</tr>
</tbody>
</table>

Table 2  Medication Prior to Stenting

| Aspirin (%) | 96 |
| Clopidogrel (%) | 76 |
| Statin (%) | 84 |
| ACE inhibitor (%) | 69 |
| ß-blocker (%) | 73 |

ACE, angiotensin-converting enzyme.
Methods

Patients and Lesion Population
From September 2005 until January 2007, 93 high-risk patients (110 carotid arteries) with severe carotid stenosis and 1 or more high-risk features for carotid endarterectomy were scheduled for carotid artery revascularization. Of them, 10 patients (11%; 10 carotid arteries) were primarily indicated for carotid endarterectomy and 83 patients (89%; 100 carotid arteries) for endovascular treatment (DCAS). Standard institutional eligibility criteria for revascularization during the study period were: symptomatic patients with stenosis >50% and asymptomatic patients with stenosis >70% of either the common or internal carotid artery. Patients with restenosis were excluded. Stenoses were quantified according to the NASCET criteria.7 Clinical criteria for high-risk patients included: need for open heart surgery, history of open heart surgery, history of myocardial infarction, known multivessel coronary artery disease, left ventricular dysfunction (ejection fraction ≤40%), severe pulmonary or renal disease, significant contralateral carotid disease, previous endarterectomy, age ≥80 years. Tables 1 and 2 summarize the baseline demographic and clinical characteristics of percutaneously treated patients. All patients gave written informed consent prior to procedure. Analysis was by intention-to-treat.

Stenting Procedure and Postprocedural Protocol
All procedures were performed via the femoral approach using a 7 or 8Fr guiding catheter or guiding sheath. After baseline angiography was performed (Fig 1), the intervention (J.V.) chose 1 of 2 distal protection filter devices (Filter...
Wire EZ, Boston Scientific, Mountain View, CA, USA (90 procedures) or Angioguard, Cordis, Johnson & Johnson, Miami, FL, USA (10 procedures)). Filter Wire was the first choice, but Angioguard was used when the diameter of the internal carotid artery was more than 5.5 mm. DCAS was performed using self-expanding stents: Precise RX (Cordis, Johnson & Johnson; 60 stents); Carotid Wallstent Monorail (Boston Scientific, Galway, Ireland; 31 stents); NexoStent (EndoTex Interventional Systems, Inc, Cupertino, CA, USA; 4 stents); Xact (Abbott Vascular, Galway, Ireland; 4 stents); and Sinus-Carotid-RX-System (Optimed, Ettingen, Germany; 4 stents) (Figs 2, 3). The passage of the stent to the desired position at the lesion site was attempted with moderate push and, if necessary, with deep intubation of the guiding catheter. In the case of angled origin of the common carotid artery (type III or bovine arch) the Hockey stick, Amplatz right or Amplatz left guiding 8Fr catheter was the first choice. In such cases, the tip of the catheter was usually positioned in the proximal segment of the common carotid artery to reduce the risk of embolization, although this approach generally provides less support for the procedure.

If this approach was not successful, the lesion was dilated with a coronary angioplasty balloon before stenting. After stent deployment, postdilation was performed with a balloon matched to the distal reference vessel diameter in order to achieve optimal stenting result (nominal balloon diameter 4–7 mm, inflation pressure 6–12 atm, a balloon: internal carotid artery ratio of 0.6:0.8) (Fig 4). Residual stenosis less than 30%, absence of an uncovered intimal dissection and nonlimited flow were considered to constitute a satisfactory result (Fig 5). Asymptomatic patients after uncomplicated procedure were discharged the next day. All patients were prospectively asked to undergo clinical 30-day follow-up. The occurrence of major clinical events (death, stroke, transient ischemic attack, myocardial infarction or clinically driven carotid artery revascularization) was recorded.

Medical Treatment

The anticoagulant and antithrombotic protocol comprised administration of 200–500 mg of aspirin and clopidogrel 300 mg at least 24 h before the procedure. Intra-arterial administration of a heparin bolus at the beginning of the procedure (70–100 IU/kg body weight) maintained an activation clotting time of 250–300 s. Glycoprotein IIb/IIIa inhibitors were not used. Atropine 0.5–1 mg intravenously was used prior to postdilation in patients with a heart rate less than 60 beats/min. Patients were discharged on dual antiplatelet therapy (aspirin 100 mg and clopidogrel 75 mg/day) and aspirin was continued indefinitely.

Definitions

Patients underwent complete clinical (including neurological) examination before and after the procedure and at 30-day follow-up. Stroke was defined as a neurological deficit that persisted more than 24 h; minor stroke was defined as a new neurological deficit that resolved completely or returned to baseline within 30 days. Transient ischemic attack was defined as a new neurological deficit that persisted for less than 24 h and completely resolved or returned to baseline. Major adverse events (primary endpoint) were death, stroke, transient ischemic attack, clinically driven carotid artery revascularization or myocardial infarction.

Statistical Analysis

Microsoft Excel with Analyse-It (Analyse-it Software, Ltd, UK) was used for the study database and its analysis. Continuous variables are expressed as mean±SD, categorical variables as counts and percentages. Fluoroscopic time is presented as median and range.

Results

Immediate Outcome

All patients had technically successful stenting procedures using distal filter protection. Predilation was necessary in 1 (1%) procedure. The mean percent diameter stenosis (NASCET) was reduced from 80±9% to 7±9%. Four patients developed neurological symptoms immediately post dilation; symptoms resolved in 3 patients within 24 h (transient ischemic attack) and in 1 patient within 2 weeks (minor stroke). One patient developed symptoms 2 h after procedure, but these resolved within 1 week. No cardiovascular or neurological events occurred during either the procedure or the observation period in the remaining patients. Transient bradycardia occurred during 24% of procedures, but sustained hemodynamic instability did not occur in any of the patients. Table 3 summarizes the interventional and angiographic characteristics.

Short-Term Follow-up

All patients were examined 30 days after procedure. One patient developed a minor stroke during the early postprocedural period, but the remaining patients were asymptomatic. There were no deaths, myocardial infarctions, repeat procedures or access site complications. The outcomes of short-term follow-up are summarized in Table 4.

Discussion

This is the first study to demonstrate the feasibility and safety of DCAS with a protective filter device in a population of 83 high-risk consecutive patients (100 carotid arteri-
ies) scheduled for endovascular treatment. The primary success rate of stenting was 100%, predilation was needed in 1 case (1%), median fluoroscopic time was 7 min, and the 30-day major adverse event rate was 6%.

The major complication of DCAS is related to embolization of atherosclerotic debris into the cerebral circulation during the procedure, resulting in stroke. Unfortunately, as has been shown recently by Verzini et al, a large number of complications can occur also outside the window of emboli protection device use (in 2% of procedures in the present study). Despite the high-risk features of the consecutive patients described here, the procedural and follow-up results are favorable and comparable with previously published surgical results in low-risk patients or in high-risk-patient endovascular trials.

The most important factor in achieving technical success in DCAS is being able to gain access to the common carotid artery through a long guiding sheath or guiding catheter. A guiding sheath positioned in the common carotid artery ensures greater support for completing the direct stenting procedure. However, we prefer the technique of the guiding catheter, which is simpler, although it has a theoretical increased embolization risk in cases of aortic arch or a common carotid artery with severely diseased vessel wall. In the present study, the guiding catheter technique was used in most cases (90%) and either a Multipurpose or Judkins right guiding catheter was used. In the case of a very angled origin of the common carotid artery (type III or bovine arch) the Hockey stick, Amplatz right or Amplatz left guiding 8Fr catheter was the first choice.

We believe our findings are important because first, the present study comprised a consecutive high-risk patients treated percutaneously were shown to be good candidates for DCAS (predilation was necessary only in 1 case), and their short-term clinical outcomes were comparable with those in previously published studies. In the SAPPHIRE study, which involved high-risk patients, the early (up to 30 days) cumulative incidence of stroke, myocardial infarction, or death was 4.8% among patients assigned to receive a stent. In the BEACH trial, which evaluated the outcome of CAS in patients at high surgical risk for endarterectomy, the 30-day incidence of stroke, death, and myocardial infarction was 5.8%. Similarly, in the CREATE trial, the primary endpoint (death, stroke, myocardial infarction) occurred in 6.2% of patients during a 30 day follow-up. In the SPACE study, the primary endpoint (30-day follow-up: death or a stroke lasting more 24 h) occurred in 6.8% of initially symptomatic patients.

In the present study, the occurrence of the primary endpoint (death, stroke, myocardial infarction, and clinically driven target lesion revascularization) at 30 days was 6%. It is notable that in the recently published study, EVA-3S, the 30-day incidence of any stroke or death in the high-risk symptomatic patients was 9.6% after CAS. However, we believe that those unacceptable results were caused by poor training of the interventional physicians (prior to study, they had to have performed only 12 CAS procedures or 35 procedures in supra-aortic trunks, of which at least 5 had to be in the carotid artery). Third, all of the present procedures were performed with commercially available stents, and with regard to direct stenting we did not find any significant differences among the different stents used.

We consider that DCAS has potential advantages in terms of shortened procedural time, decreased radiation and contrast medium load received by the patient and decreased cost of the procedure. On the other hand, DCAS may be associated with some potential complications. First, DCAS may require more aggressive deep seating and manipulation of the guiding catheter (sheath) than would be necessary if balloon predilation was performed. However, using either the guiding or the guiding sheath technique, carotid artery trauma did not occur in the present study. Thus, based on our experience, we would attempt the direct approach in all patients referred for carotid stenting. Second, we should take in account that in case of intervention of a tight lesion, the ability of exact stent positioning is decreased, because blood flow is considerably compromised by stent. Fortunately, the surrounding skeletal structures simplify correct positioning and subsequent exact stent implantation. Third, the passage of the stent to the desired position at the lesion site is associated with plaque trauma that could result in an increased probability of embolization, mainly in patients with echolucent (vulnerable) plaques. However, in the present study the clinically relevant embolization rate was acceptably low and, moreover, we did not have any patient experience an ischemic event associated immediately with catheter or stent passage. Fourth, theoretically, after stent deployment in a heavily calcified lesion we could fail to expand the stent by balloon dilatation, which could result in problems with filter device extraction. In this study, we did not experience such a case.

**Conclusion**

The main finding that emerges from this single-center registry is that DCAS is a feasible, safe, and ultra-short procedure in high-risk patients scheduled for carotid stenting procedure. Additionally, the results suggest the aggressive approach in indication to endovascular therapy (and only exceptional indication to carotid endarterectomy) might be feasible and safe. However, a prospective study is needed to test this hypothesis.

**Acknowledgment**

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**References**


