Carotid Recanalization in Nonacute Internal Carotid Artery Occlusion: A Therapeutic Option for Ischemic Stroke

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IPsilateral chronic carotid occlusion (CCO) can be found in up to 15% of patients with transient ischemic attacks (TIAs) and strokes.1,2 Cervical occlusion is a morbid diagnosis with a high risk (6%-20%) of recurrent strokes and ipsilateral strokes (2%-9.5%).3-5 The subgroup of patients with severe hemodynamic compromise with CCO is at a higher risk for such events.6

The effectiveness of percutaneous transluminal angioplasty and stenting of the extracranial carotid artery is improving as a result of the development of autoexpandable prostheses and new systems of cerebral protection.7 Currently, this technique constitutes a true alternative to carotid endarterectomy in the treatment of a severe degree of carotid stenosis with a minimum risk of cerebral embolization.8-10 We attempted endovascular recanalization in select patients with CCO and retrograde ophthalmic artery flow.11 We present an early report on the safety and efficacy of endovascular recanalization in symptomatic CCO. In this study, we evaluate the safety and efficacy of endovascular recanalization in CCO with severe hemodynamic compromise.

METHODS

We performed a retrospective review of patients with symptomatic CCO. We identified 39 patients with CCO who were admitted to our institution after suffering an ischemic event, stroke, or TIA. Neurological evaluation included preprocedural and postprocedural clinical examination and neuropsychological tests.12 In addition to routine neurological examinations, we focused on cognitive function. We used the Rankin Scale to measure disability scores, the National Institutes of Health Stroke Scale to detect focal disorder, and the Barthel Scale to evaluate functional incapacity. Minor stroke was defined as an increase in the National Institutes of Health Stroke Scale score of < 3 with complete resolution or no significant disability at 30 days. Major stroke was defined as an increase in the National Institutes of Health Stroke Scale score of ≥ 3 with significant disability at 30 days.

Neuropsychological tests included global cognitive function (Mini-Mental State Examination of Folstein, Information-Memory-Concentration of Blessed), specific cognitive function (Wechsler Adult Intelligence Scale, Wechsler Memory Scale, clock test, etc), and emotional status (profile of mood state). All the patients underwent a preliminary cerebral computed tomography (CT) scan or magnetic resonance imaging and vascular exploration of supra-aortic vessels (ultrasound, magnetic resonance angiography, and arteriography).

Preprocedural Medication

All patients were prescribed a double antiplatelet therapy with clopidogrel 75 mg and aspirin 300 mg per day at initial diagnosis. During angioplasty, we administered atropine 1 mg IV to avoid bradycardia resulting from manipulation of the carotid glomus. Heparin was administered to obtain an activated clotting time of ≥ 250 seconds at 70 IU/kg. After the procedure, an infusion of 10,000 IU heparin/24 h was maintained to reduce embolic/thrombotic complications. The procedure was performed under local anesthesia and intravenous sedation.

Technique

A femoral approach with an 8F or 7F sheath placed in the right femoral artery was used. A 5F pigtail catheter was advanced as far as the aortic arch to perform a complete brachiocephalic vessel study. This was followed by a cerebral parenchymography study with the injection of 40 cm³ contrast at 20 cm³/s (Figure 1A).13 A 5F Terumo (Terumo Medical Corp, Somerset, New Jersey) catheter in the common carotid artery was used to perform anteroposterior and lateral projection digital subtraction angiograms of the cervical and intracranial internal carotid artery (ICA; Figure 2A).

Recanalization was attempted when a flow reversal was detected in the proximal portion of the carotid siphon via the ipsilateral ophthalmic artery from its external carotid artery anastomoses. An 8F or a 7F guide Cordis catheter (Cordis Corp, Miami Lakes, Florida) was advanced to the common carotid artery over an interchange guidewire placed in the external carotid artery. Frequently, a small angiographic irregularity was observed at the proximal site of the ICA occlusion. This angiographic irregularity was used as a guide to identify the course of the immediately distal occluded vessel (Figure 3A). Urokinase (200-300 IU) or tissue
FIGURE 1. A, full dynamic digital parenchymography sequence before left internal carotid artery recanalization showing nonfilling of its cervical, intrapetrosal, and cavernous segments. There is some collateral filling of the left anterior and posterior cerebral arteries through the circle of Willis, but a clear hemodynamic insufficiency at the distal territory of these 2 arteries is observed. B, postrecanalization parenchymography run demonstrating good recuperation of the hypoperfused area with some expected “hyperhemic” response at the same level.
plasminogen activator (10 mg) was administered through the guide catheter before the recanalization maneuver was begun. Aspiration was performed after waiting for 10 minutes before the deployment of the microguidewire.

Using a roadmap from the guide catheter, a 0.014-in microguidewire is used to traverse the occluded segment of the vessel. In our experience, when the guidewire progresses without undue resistance, with careful maneuvering, it stays within the true lumen of the occluded vessel. Once the guidewire reaches the distal portion of the cervical ICA, a microcatheter is advanced and an angiography is performed to confirm the true lumen distally. A predilatation procedure is done with a $2 \times 20$-mm angioplasty balloon to reform the lumen of the vessel (Figure 3B). A cerebral protection device (filter or balloon) is gently progressed through this lumen (Figure 3C). A self-expandable endoprosthesis is deployed in the ICA and across the bifurcation (Figure 3D). Postdilatation of the stent is then performed with a 4 to 6 $\times 20$-mm, 0.014-in wire-compatible balloon (Figure 3E).

At the end of the procedure, the cerebral protection device is removed from the artery, and a control run is performed (Figure 2B). Finally, a 5F pigtail catheter is
introduced and a control cerebral digital dynamic parenchymography is performed (Figure 1B). All patients are admitted to the intensive care unit for 24 to 48 hours where the hemodynamic parameters are closely monitored.

RESULTS

We attempted recanalization of nonacute ICA occlusion in 39 patients. One patient had bilateral lesions that were treated, bringing the total to 40 lesions. Twenty-six patients (66%) were men; the age range was 36 to 79 years. The left ICA was occluded in 30 cases (75%). The most usual initial clinical syndrome was ischemic stroke (58.3%), followed by TIA (41.7%). The most important risk factors were arterial hypertension and tobacco abuse (50%), dyslipidemia (30%), and diabetes mellitus (20%).

Recanalization was attempted in a nonacute setting. The procedure was attempted on average 7.1 weeks (range, 2-35 weeks) after the initial presentation. We obtained complete recanalization in 34 cases (87%). The procedure was unsuccessful in 5 (12%). In 4 cases (10%), it was not possible to traverse the occluded segment with the microguidewire, and 1 patient (3%) had an acute intrastent thrombosis. These 5 patients had the onset of carotid occlusion > 6 months before the procedure, and they remained asymptomatic after the procedure. None of the patients reported any new-onset symptoms. In no case did we observe carotid dissection or evidence of distal embolic events. In the postprocedural period, the patients routinely remained in the intensive care unit for 24 hours. During this time, hemodynamic monitoring did not reveal any patient with evidence of reperfusion syndrome.

Clinical and radiographic follow-up has ranged from 6 months to 4 years (mean, 2.2 years). The patients were followed with carotid ultrasounds at 3, 6, and 12 months. During the first 6 months, double antiplatelet therapy with aspirin and clopidogrel was prescribed to all patients. After 6 months, a single antiplatelet therapy was prescribed. Regular supra-aortic Doppler studies have shown carotid patency in all patients who had successful recanalization. In addition, none of these patients suffered a new ischemic event during follow-up.

DISCUSSION

Approximately 15,000 to 20,000 cases of new-onset symptomatic carotid occlusion occur annually in the United States. The overall incidence rate is 6 per 100,000 with the highest rate (40 per 100,000) seen in older men (≥65 years of age).3 In recent-onset carotid occlusions, exhausted cerebrovascular reactivity leads to early disabling strokes.5 The annual rate of symptomatic stroke in patients with ranges from 2.4% to 7%.3-5,12 Although large-scale studies are lacking, recent publications have reported successful recanalization of CCO. The reported studies (Table) have included from 8 to 30 patients with a success rate of recanalization procedures ranging from 73% to 88%.15-22 The largest series of successfully recanalized patients has been reported by Kao et al.14 They were able to achieve successful recanalization in 22 patients with 1 death and no strokes at follow-up. They did report in-stent stenosis in 13.6%. We report our experience in a group of 27 patients with a success rate of 81%. We were able to achieve durable recanalization in 22 patients with no strokes or mortality at follow-up. Acute in-stent thrombosis was seen in 1 patient, as was reported by Kao et al.14 Other complications have been reported, including transient paresis and middle cerebral artery branch occlusion, but were not seen in our patient cohort.19,20 Terada et al19 have reported various potential problems, including postrecanalization hyperperfusion syndrome, cerebral embolism during treatment, durability of treatment, and difficulty in identification of the occlusion point. We did not find any evidence of hyperperfusion syndrome or intracranial hemorrhage in our patients.

Patient Selection

Patients with CCO are not a homogeneous group with equivalent risk factors for symptomatic strokes. Subgroup analysis of patients with CCO reveals that some patients are at a higher risk for vascular events. Flaherty et al3 have elucidated a temporal trend in the incidence of symptomatic stroke. In their study, early (1 year) rates of symptomatic strokes were as high as 10%, and 5-year rates ranged from 5% to 22%.5 In a study of recent-onset carotid occlusion, the risk of early new-onset stroke increased to 27% from 5.5% with exhausted cerebrovascular reactivity as determined by Doppler CO2 test. Stage II failure as determined by positron emission tomography is shown to confer a relative risk of 7.3 for ipsilateral stroke in patients with CCO.5 We believe that it is essential to demonstrate hemodynamic failure to select patients with a higher risk who may benefit from recanalization of occluded carotid artery. We performed digital dynamic parenchymography in all patients before attempting recanalization procedures. Parenchymography is a powerful real-time tool to study hemodynamic reserve in ipsilateral carotid occlusive disease. During the capillary phase, hypoperfusion in the watershed region is correlated with the degree of carotid stenosis.21 In addition, a delay in filling is observed in the ipsilateral hemisphere associated with vascular stasis in the intermediate and venous phases. Once recanalization was performed successfully, immediate normalization of intracranial blood flow was demonstrated in all such patients. In addition to helping select patients with a higher risk, parenchymography allows such a comparison of preprocedural and postprocedural hemodynamic state.13 Reversal of ophthalmic artery flow direction is a good marker for hemodynamic insufficiency caused by proximal ICA stenosis.16 In our patients, ophthalmic artery documented flow reversal was a prerequisite for any attempts at recanalization. We believe that this flow reversal, at least in theory, affords protection from cerebral embolic events during the microguidewire maneuvers and during the predilatation stage.

In studies reporting recanalization of CCO, the authors report strict hemodynamic screening before attempting the procedure. Recurrent or progressive ipsilateral symptoms have been reported as an important indication for recanalization.14-17,19 Other authors have relied on specific modalities like CT perfusion,16,17,21 acetazolamide stress 133Xe CT,16 single-photon emission CT, and single-photon emission CT

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## TABLE. Articles Reporting on Recanalization of Chronic Carotid Occlusion

<table>
<thead>
<tr>
<th>Study</th>
<th>Date</th>
<th>Total Patients (Lesions), n</th>
<th>Hemodynamic Selection</th>
<th>Flow Reversal (%)</th>
<th>Distal Embolic Protection Device (%)</th>
<th>Successful Recanalization, n (%)</th>
<th>Mean Time to Follow-up (Range), mo</th>
<th>New Ipsilateral Neurological Deficits or TIA</th>
<th>Nonacute In-Stent Reocclusion, n (%)</th>
<th>Other Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terada et al15</td>
<td>March 2005</td>
<td>1</td>
<td>SPECT with acetazolamide challenge</td>
<td>Yes</td>
<td>No</td>
<td>1 (100)</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>Kao et al16</td>
<td>March 2007</td>
<td>30 (30)</td>
<td>Progression or recurrence of neurologic deficit (83), hemisphere ischemia by perfusion CT or acetazolamide stress (17)</td>
<td>No</td>
<td>Yes (77)</td>
<td>22 (73)</td>
<td>16.1 ± 18.5 (n = 26)</td>
<td>0</td>
<td>3 (13.6)</td>
<td>Fatal nonipsilateral stroke (3.3)</td>
</tr>
<tr>
<td>Lin et al17</td>
<td>October 2008</td>
<td>54 (54)</td>
<td>Progression or recurrence of neurologic deficit (69), hemisphere ischemia by perfusion CT (31)</td>
<td>No</td>
<td>Yes (73)</td>
<td>35 (65)</td>
<td>3 (minimum) for all (n = 54)</td>
<td>1 (2%)</td>
<td>2 (5)</td>
<td>Nonipsilateral stroke (2), death (2)</td>
</tr>
<tr>
<td>Shojima et al18</td>
<td>March 2010</td>
<td>8 (8)</td>
<td>SPECT with acetazolamide challenge</td>
<td>Yes</td>
<td>Yes</td>
<td>7 (88)</td>
<td>19.4 (9-32) (n = 8)</td>
<td>0</td>
<td>1 (12)</td>
<td>Retinal hemorrhage (12), groin hematoma (12)</td>
</tr>
<tr>
<td>Terada et al19</td>
<td>March 2010</td>
<td>14 (15)</td>
<td>SPECT with acetazolamide challenge (66), recurrent symptoms (33)</td>
<td>Yes</td>
<td>No</td>
<td>14 (93)</td>
<td>26.1 (2-56) (n = 15)</td>
<td>0</td>
<td>0</td>
<td>Dissection (26), embolism (6)</td>
</tr>
<tr>
<td>Puech-Leão et al20</td>
<td>April 2010</td>
<td>16 (16)</td>
<td>New TIA or stroke</td>
<td>No</td>
<td>Yes (100)</td>
<td>13 (81)</td>
<td>20.4 (10-30) (n = 16)</td>
<td>0</td>
<td>0</td>
<td>Transient hemiparesis (6)</td>
</tr>
<tr>
<td>Hauck et al21</td>
<td>October 2010</td>
<td>2</td>
<td>CT perfusion (50), new TIA (50)</td>
<td>No (50), yes (50)</td>
<td>No</td>
<td>2 (100)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Transient hemiparesis (6)</td>
</tr>
<tr>
<td>Takagi et al22</td>
<td>November 2010</td>
<td>1</td>
<td>SPECT</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>9</td>
<td>0</td>
<td>1</td>
<td>MR change</td>
</tr>
<tr>
<td>This study</td>
<td>...</td>
<td>39 (40)</td>
<td>Parenchymography, documented ophthalmic flow reversal</td>
<td>No</td>
<td>Yes (100)</td>
<td>34 (87)</td>
<td>15 (6-24) (n = 39)</td>
<td>0</td>
<td>1 (3)</td>
<td></td>
</tr>
</tbody>
</table>

*CT, computed tomography; MR, magnetic resonance; SPECT, single-photon emission computed tomography; TIA, transient ischemic attack. The results of existing English language literature indexed in PubMed are tabulated.*
with acetazolamide challenge.\textsuperscript{15,18,19} We believe that strict hemodynamic selection may be related to the negligible incidence of reperfusion syndrome seen in our group and in other reported studies on recanalization of CCO (Table). This is in contrast to the 2% to 5% reported incidence of symptomatic acute reperfusion syndrome in the carotid stenosis series.\textsuperscript{24} Although contralateral CCO has been reported as an independent predictor,\textsuperscript{25} recanalization of ipsilateral CCO does not appear to predispose patients to reperfusion injury. Larger, prospective studies are needed to address this phenomenon adequately.

### Timing of Vascular Rescue

Analysis of the failed recanalization attempts revealed that all were CCO patients with documented occlusion dating \(\geq 6\) months. We also observed that our recanalization attempts were more successful when made 2 to 6 weeks after the initial diagnosis of occlusion. In addition to offering a greater chance of successful recanalization, these patients were in the high-risk group for ipsilateral strokes as reported by Flaherty et al.\textsuperscript{5} We propose that early recanalization attempts will both increase the chance of technical success and afford protection to the highest risk group of patients with CCO.

### Absence of Acute Secondary Cerebral Embolism

The progression from severe carotid stenosis to complete occlusion occurs in up to 10% of patients. Reduced poststenotic peak systolic velocity is highly predictive of the progression of occlusion in such patients. Other factors that predict the onset of occlusion include poststenotic arterial narrowing and very severe stenosis.\textsuperscript{8} We speculate that a severe reduction in flow and arterial wall collapse leads to thrombosis of the lumen. If thrombosis of the lumen were the sole reason for CCO (with no arterial wall collapse), secondary embolic phenomenon would be expected before the deployment of a cerebral protection device. We did not encounter any evidence of secondary cerebral embolism during the microguidewire advancement and the predilatation phase. This observation appears to suggest that arterial wall collapse may in fact play a major role in CCO owing to the progressive reduction of flow in the lumen.

Flow reversal techniques have been used during recanalization procedures to prevent potential anterograde cerebral embolism. Use of Parodi and modified Parodi systems has been reported.\textsuperscript{15,18,19} We chose not to use flow reversal systems because we had strict criteria for selecting only those patients who demonstrated reversal of flow at the carotid siphon. Theoretically, such a “natural” flow reversal would prevent any anterograde embolism until anterograde flow is restored after recanalization. To prevent anterograde embolism after lesion crossing, we used distal cerebral embolic protection devices in all our patients. Currently, there appears to be no consensus on the use of such devices. Distal embolic protection devices are used either inconsistently\textsuperscript{16,17} or not at all.\textsuperscript{15,19,21,22} However, it must be emphasized that even with consistent use of such devices, neurologic injury is still possible.\textsuperscript{20}

### Safety of the Procedure

Arterial rupture and cerebral ischemic injuries have been reported in endovascular manoeuvres.\textsuperscript{20} In our patients with CCO, we did not see any ischemic events or transgression of the arterial wall. We propose that the technique as described is safe and should be considered a therapeutic option in certain patients with nonacute carotid occlusion. We further propose that successful recanalization leads to durable protection from new ischemic episodes. A review of the literature reveals that the safety record of this procedure is being established through small reported studies (Table). Reported procedural complications include dissection of the carotid and groin hematoma. The rate of successful recanalization appears to vary between 73% and 93%. From the available data, there are no clear statistical trends to predict failure of recanalization rate. From the results in our patient group, we have hypothesized that occlusion \(\geq 6\) months may be a predictor of failure. In the study by Terada et al,\textsuperscript{19} no such temporal trends were seen. Larger, prospective trials would assist in developing clear guidelines regarding the indications for recanalization of CCO. After successful recanalization, none of these studies reported evidence of hyperperfusion syndrome. However, Shojima et al\textsuperscript{18} reported evidence of acute asymptomatic diffusion-weighted imaging lesion, and Puech-Léao et al\textsuperscript{20} reported 1 case of transient hemiparesis.

### Durable Protection From Ipsilateral Stroke/TIA

A review of reported studies reveals a high degree of effectiveness of recanalization procedures in preventing recurrent ipsilateral strokes and TIAs. Except for 1 incidence of transient hemiparesis, we did not find any reports of new ipsilateral strokes or TIAs after recanalization of CCO (Table). In our group, the procedure appeared to afford complete protection from new-onset stroke or TIA. Because the natural history of CCO has a 2.4% to 7% annual incidence of ipsilateral strokes, we find this reduction to be quite a powerful argument in favor of recanalization procedures. Furthermore, this protection appears to be durable. Nonacute in-stent stenosis rates between 5% and 13% have been reported.\textsuperscript{16-18} In our group, 1 patient (3%) had a reocclusion resulting from thrombosis. Most authors, including us, report that a second recanalization procedure led to durable patency in these cases.

### CONCLUSIONS

Learning from our early results, we propose that carotid recanalization is a viable option for symptomatic patients with CCO and severe hemodynamic compromise. As described, the procedure was successfully performed in 81% of our patients with no major complications. However, this technique requires that the operators have great experience in endovascular carotid pathology treatment. Long-term follow-up has shown the persistence of carotid blood flow and absence of new cerebral ischemic events. Larger, prospective studies would help us clearly identify the indications for endovascular recanalization in CCO.
Disclosure
The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES