Management of Patients With Concomitant Severe Coronary and Carotid Artery Disease

Is There a Perfect Solution?

Marco Roffi, MD

Despite limited evidence of the benefit of carotid revascularization before or together with coronary artery bypass grafting (CABG), patients with advanced carotid and coronary disease are frequently treated by a combined or staged carotid/coronary surgical revascularization. In the present issue of Circulation, investigators from Nieuwegein in the Netherlands describe in a large group of patients an alternative revascularization approach: carotid artery stenting (CAS) followed by CABG. The rate of death, stroke, or myocardial infarction (MI) from the time of CAS to 30 days after cardiac surgery (6.8%) compares well with previous surgical series (Table). The associated neurological complication rates were low both at 30 days (major ipsilateral stroke 1.1%) and at a mean follow-up of 31 months (neurological death 1.1% and major ipsilateral stroke 1.1%). The carotid restenosis rate was negligible. The authors must be commended for the favorable patient outcomes and for the volume of procedures performed (47 per year), which are superior to most, if not all, recent surgical series of combined coronary-carotid revascularization (Table). Additional important aspects of the study were that patients were accepted for CAS by a consensus decision that involved neurologists, surgeons, and interventionists and that neurologists were deeply involved in the care of those patients throughout the hospital stay.

With respect to the surgical management of concomitant coronary and carotid disease, a systematic review of the studies published up to 2002 showed that the overall 30-day rate of death, stroke, or MI was 11%. Several single-center experiences have followed, documenting a death rate ranging between 3.6% and 6.1% and a stroke rate between 2.8% and 5.5% up to 30 days (Table). A population-based analysis performed in the United States detected a combined death and stroke rate of 17.7% among 226 procedures. Among 744 patients extracted from the New York Cardiac Database, the combined death and stroke rate was 8.1%. An analysis of all combined surgical procedures performed in Canada, with the exception of the province of Quebec, detected an in-hospital mortality rate of 4.9% and a postoperative stroke rate of 8.5%. Finally, using the Nationwide Inpatient Sample, an in-hospital death or stroke rate of 9.7% was reported among 7073 patients treated with carotid endarterectomy (CEA) and CABG. According to the American Heart Association, the decision to perform CEA in patients with asymptomatic carotid stenosis >70% that requires CABG is “uncertain.” The recent American Academy of Neurology recommendations on CEA stated that “the available data are insufficient to declare either CEA before or simultaneous with CABG as superior [to a conservative carotid management] in patients with concomitant carotid and coronary occlusive disease.”

The concept of performing CAS before open heart surgery is not novel. In a retrospective analysis, investigators at the Cleveland Clinic in Ohio compared the outcomes of patients undergoing CAS before open heart surgery (n=56) and those undergoing a combined surgical approach (n=111) and showed favorable results for the partially endovascular approach. The analysis was limited by imbalances among the groups: more unstable/severe angina, severe left ventricular dysfunction, symptomatic carotid disease, and need for repeat open heart surgery in the CAS group; more severe contralateral carotid disease in the group treated only surgically. The incidence of death, stroke, or MI 30 days after open heart surgery was 10.7% in the CAS group and 21.6% in the surgical group (P=0.08; Table). Investigators in Sheffield, United Kingdom, performed a prospective study on 52 patients undergoing CAS followed by open heart surgery. Despite the lack of periprocedural neurological events after CAS, 3 patients died of cardiac causes while awaiting surgery, and 6 had complications related to surgery, for a total death or stroke rate at 30 days after CABG of 19.2%. A group from Sydney, Australia, reported a death, stroke, or MI rate of 10% among 20 patients undergoing staged CAS-CABG.

Unresolved issues include the minimal delay required between CAS and open heart surgery and the antiplatelet regimen at the time of CABG. Although the need for urgent cardiac surgery was not an exclusion criteria in the present study, and approximately one third of the patients had unstable angina, the patients were “planned for CAS and cardiac surgery.” Individuals with uncontrolled cardiac symptoms may have undergone urgent combined surgery. Therefore, the described strategy may not apply to those patients. In the study, all patients received dual-antiplatelet therapy at the time of CAS, and “aspirin and clopidogrel were discontinued.
5 days before surgery, if possible.” Although it is unclear why aspirin discontinuation was recommended, the antiplatelet regimen at the time of CABG was not detailed. The authors described that the mean time to cardiac surgery was 22 days and that approximately one third of patients underwent CABG within 14 days, one third between 14 days and 1 month, and one third after 1 month. Encouraging in this respect was the lack of carotid stent thrombosis reported.

A group in Chicago, Ill, reported no deaths or neurological events among 37 patients treated with CAS who underwent CABG within 48 hours.19 The antithrombotic regimen during and after CAS consisted of unfractionated heparin and the glycoprotein IIb/IIIa receptor antagonist eptifibatide, the latter for up to 6 hours before CABG. A recent study from Buenos Aires, Argentina, showed the feasibility of another approach, namely, concurrent CAS and open heart surgery.15 The endovascular procedure was performed after the administration of aspirin and unfractionated heparin, and patients (n=30) were transferred from the catheterization laboratories to the operating room. Clopidogrel was added after surgery if the patient had no postoperative bleeding. No strokes or neurological deaths were observed. The same strategy was also associated with no strokes or deaths among 10 patients treated in Rome, Italy.16

The role of best medical treatment as an alternative to revascularization in patients with asymptomatic carotid stenosis, as well as secondary prevention after carotid revascularization, needs to be elucidated. A broad disease-management approach based on lifestyle modification, statin therapy, and optimal blood pressure control, preferably with an angiotensin-converting–enzyme inhibitor, is more likely to affect both the quality and duration of life than carotid revascularization itself. This aspect is critical, because after CEA, patients remain at a higher long-term risk of (cardiac) death.20

The differential role of carotid disease and ascending aorta atherosclerosis as underlying mechanisms of stroke among patients with advanced carotid and coronary disease who are undergoing cardiac surgery needs to be elucidated. The question is whether the focus is on the wrong culprit (carotid stenosis) instead of addressing the true (and difficult to treat) source of embolism, namely, the ascending aorta.21 Although stroke risk during CABG has been related to the degree of carotid stenosis, it has been estimated that more than half of all territorial infarctions on CT scan or autopsy are not related to carotid disease alone.22 Unfortunately, despite the increasing amount of evidence in the literature that points to ascending aorta atherosclerosis as a critical culprit in the pathogenesis of post-CABG stroke, most cardiac surgery databases do not track prospectively the extent of atherosclerotic disease in the ascending aorta.23

How can we identify the best management strategy (optimal medical therapy, endarterectomy, or stent) for patients with severe asymptomatic carotid stenosis that requires open heart surgery? The perfect but unrealistic solution would be a randomized trial; however, the target population is too small. In a nationwide US survey, among the population of patients undergoing CABG, those undergoing combined CEA-CABG accounted for only 1.1% in 1993 and 1.6% in 2002.6 Even lower was the proportion of combined CEA-CABG compared with CABG in a recent Canadian survey (0.5%).4 Finally, high-volume centers report between 13 and 30 combined surgical procedures per year (Table). A randomized trial testing noninferiority between CABG only, CEA-CABG, and CAS followed by CABG would be relevant clinically. However, given the assumption of a 30-day death,

### Table. Outcomes up to 30 Days for Patients Undergoing CEA and CABG or CAS Followed by CABG

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients per Year, n</th>
<th>Death, %</th>
<th>Stroke, %</th>
<th>MI, %</th>
<th>Death/Stroke, %</th>
<th>Death/Stroke/MI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CEA–CABG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systematic review 1972–20022</td>
<td>8972</td>
<td>N/A</td>
<td>4.5</td>
<td>4.5</td>
<td>3.9</td>
<td>8.4</td>
</tr>
<tr>
<td>Liège, Belgium3</td>
<td>311</td>
<td>22</td>
<td>6.1</td>
<td>5.5</td>
<td>2.2</td>
<td>11.6</td>
</tr>
<tr>
<td>Canada4</td>
<td>669</td>
<td>N/A</td>
<td>4.9</td>
<td>8.5</td>
<td>N/A</td>
<td>13.0</td>
</tr>
<tr>
<td>Medicare6</td>
<td>226</td>
<td>6.6</td>
<td>12.0</td>
<td>N/A</td>
<td>17.7</td>
<td>N/A</td>
</tr>
<tr>
<td>US nationwide inpatient sample</td>
<td>7073</td>
<td>N/A</td>
<td>5.6</td>
<td>4.9</td>
<td>N/A</td>
<td>9.7</td>
</tr>
<tr>
<td>Albany, NY7</td>
<td>702</td>
<td>28</td>
<td>N/A</td>
<td>N/A</td>
<td>4.4</td>
<td>N/A</td>
</tr>
<tr>
<td>Houston, Tex4</td>
<td>277</td>
<td>12</td>
<td>3.6</td>
<td>2.8</td>
<td>0.7</td>
<td>N/A</td>
</tr>
<tr>
<td>Stony Brook, NY9</td>
<td>154</td>
<td>26</td>
<td>3.9</td>
<td>3.9</td>
<td>N/A</td>
<td>7.8</td>
</tr>
<tr>
<td>Cleveland, Ohio10</td>
<td>272</td>
<td>25</td>
<td>5.2</td>
<td>5.2</td>
<td>2.9</td>
<td>N/A</td>
</tr>
<tr>
<td>New York State Cardiac Database11</td>
<td>744</td>
<td>N/A</td>
<td>4.4</td>
<td>5.1</td>
<td>N/A</td>
<td>8.1</td>
</tr>
<tr>
<td><strong>CAS–CABG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleveland, Ohio12</td>
<td>56</td>
<td>10</td>
<td>5.4</td>
<td>1.8</td>
<td>3.3</td>
<td>7.1</td>
</tr>
<tr>
<td>Sydney, Australia13</td>
<td>20</td>
<td>N/A</td>
<td>0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Sheffield, United Kingdom14</td>
<td>52</td>
<td>7</td>
<td>13.5</td>
<td>5.8</td>
<td>N/A</td>
<td>19.2</td>
</tr>
<tr>
<td>Buenos Aires, Argentina15</td>
<td>30</td>
<td>3</td>
<td>10.0</td>
<td>0</td>
<td>3.3</td>
<td>10.0</td>
</tr>
<tr>
<td>Rome, Italy16</td>
<td>10</td>
<td>N/A</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nieuwegein, the Netherlands1</td>
<td>356</td>
<td>47</td>
<td>3.7</td>
<td>3.1</td>
<td>2.0</td>
<td>4.8</td>
</tr>
</tbody>
</table>

N/A indicates not applicable; MI, myocardial infarction.
stroke, or MI rate in the CEA-CABG group of 12% and a noninferiority boundary of 3%, such a study would require an enrollment of ≈4000 patients to be adequately powered. It is unlikely that this will ever take place, because even CEA versus CAS trials, which address a much broader patient population, have had to be stopped recently because of slow enrollment and lack of funding.\textsuperscript{24}

In the absence of a perfect solution, a realistic way of improving the evidence base would be to perform small, randomized studies focusing on surrogate end points, such as the occurrence of new lesions on magnetic resonance imaging or postoperative cognitive deficits. In the meantime, the best revascularization strategy for patients with advanced coronary and carotid disease should be suggested on a case-by-case basis by a multidisciplinary team that includes neurologists, surgeons, and interventionists who take into account the comorbidities of the patient, the degree of urgency of cardiac surgery, and local expertise. It would be in the best interest of these high-risk patients to be treated in high-volume centers like that in Nieuwegein.

**Disclosures**

None.

**References**


**Key Words:** Editorials ◆ arterial diseases, carotid ◆ coronary disease ◆ revascularization
Management of Patients With Concomitant Severe Coronary and Carotid Artery Disease: Is There a Perfect Solution?

Marco Roffi

Circulation. 2007;116:2002-2004
doi: 10.1161/CIRCULATIONAHA.107.735373
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/116/18/2002

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/