Obtained Objectives

The endovascular device (Wallstent) was kindly provided by Boston Scientific Inc.

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The efficacy of endarterectomy for the treatment of patients with symptomatic high-grade stenosis of the extracranial carotid artery has been established through a series of randomized, controlled trials (1–4). The absolute reduction in the occurrence of cerebral ischemic events is dependent, however, on perioperative complication rates (5,6). A combined stroke (major or minor) and death rate exceeding 6% for patients with symptomatic stenosis eliminates the benefit of stroke reduction gained through operation. Although varying according to operator and hospital experience (7), the overall incidence of major disabling stroke approaches 2% with mortality rates of <1% (8,9), thereby supporting the therapeutic advantages of carotid endarterectomy (CEA) in treating symptomatic carotid stenosis. Despite this reduction in serious complications, CEA has limitations (10–14). Minor strokes and/or complications remain significant and can be disabling. Cranial or cervical nerve palsies occur in 7.6% to 27% of patients undergoing CEA (15–17). Complications associated with concurrent cardiac disease and hypertension occur perioperatively in about 8% of patients (18). In addition, individuals with contralateral carotid occlusion or advanced coronary vascular disease are considered poor candidates for CEA (1,19–22). Other well-known anatomical considerations, which increase morbidity and mortality, include the presence of an extremely high carotid bifurcation (C1 to C2), tracheotomy, recurrent stenosis after previous CEA and radical neck dissection with or without radiation-induced carotid stenosis.

The advent of percutaneous endovascular techniques has the potential for being safer, less traumatic and more cost-effective in patients with symptomatic carotid occlusive disease. The therapeutic advantage of carotid angioplasty and stenting (CAS) has been demonstrated in patients with contralateral occlusion, restenosis and surgically inaccessible lesions (23–25). Although it has been suggested that CAS is an acceptable (26–30), if not preferred, alternative to CEA, the clinical experience has been less enthusiastic. Data accrued from various centers report a major stroke and death rate of 4.7% after CAS (30). Others report a “minor” stroke rate associated with CAS of 6.5% compared with a CEA-related risk of 0.6% (31). Although these complications may be lessened through operator experience after an as yet to be
defined “learning curve” and optimal patient selection, the
theoretical benefits of endoluminal revascularization in
treating symptomatic or asymptomatic carotid stenosis have
not been realized fully or documented in randomized
comparative trials. Indeed, the only published randomized
study of CAS versus CEA was stopped because of the
occurrence of strokes, three of which were considered major,
in five of the seven patients who underwent CAS (32).

The purpose of this prospective, randomized trial was to
compare the efficacy and benefits of CAS with CEA in the
treatment of symptomatic carotid stenosis in a community
hospital.

METHODS

This two-arm randomized clinical trial was approved by the
Institutional Review Board to include patients experiencing
symptoms and/or signs of cerebral ischemia confined to the
ipsilateral internal carotid artery. All patients were informed
that the Food and Drug Administration has not approved
deployment of stents within the carotid artery for the
treatment of carotid stenosis. Patients with symptoms of
vertebral-basilar insufficiency or intracranial occlusive dis-
ease shown by cerebral angiography were excluded. The
inclusion criteria included those sustaining events confined
to the carotid circulation within three months of evaluation;
>70% stenosis of the ipsilateral carotid bifurcation as
determined by the North American Symptomatic Carotid
Endarterectomy Trial (NASCET) (33); anticipated life
expectancy of five years; willingness to complete treatment
within two weeks and ability to sign informed consent.
Exclusion criteria included: National Institute of Health
(NIH) stroke scale of >4; cardiac arrhythmia; allergy and/or
sensitivity to aspirin, heparin, ticlopidine or clopidogrel;
history of bleeding diathesis or coagulopathy or history of
intracranial hemorrhage within two months of randomiza-
tion. A total of 104 individuals met these criteria, agreed to
participation and were selected randomly to undergo CEA
(51 individuals) or CAS (53 individuals). The presence of
contralateral total occlusion and/or the angiographic ap-
pearance of the stenotic lesion were not factors in treatment
selection. All patients received 325 mg aspirin and 75 mg
clopidogrel before CAS or CEA. A neurologist (T. C.) and
the research clinical nurse coordinator (L. B.) provided

independent oversight and neurologic examination before
and subsequent to each procedure.

Carotid endarterectomy was performed using standard
operative techniques under general anesthesia with intraop-
erative electroencephalogram monitoring. All patients were
observed in intensive care for 24 h.

Carotid angioplasty and stenting was performed using a
standard percutaneous retrograde femoral approach via
an 8F Super-S Arrowflex sheath (Arrow International, Inc.,
Reading, Pennsylvania). After heparinization with 100 μ/kg,
carotid angiography was performed with a 5F/125-cm VTK
(Cook, Inc.) catheter over a 0.035-in angled-tip glide wire.
Subsequent to guiding angiography, an 0.18-in Steel-core
wire (Guidant-ACS, Inc., Indianapolis, Indiana) was placed
in the external carotid artery for support. The Arrowflex
sheath then was advanced over either the VTK catheter or
the Arrowflex dilator into the common carotid artery.
Activated clotting time (ACT) was maintained >300.
Distal protection was not used in any case. Although not
routinely used, ReoPro (0.25 mg/kg bolus over 20 min
followed by a continuous infusion of 0.125 μg/kg/min for
12 h to a maximum of 10 μg/min) was administered to
three individuals who sustained cerebral vascular accidents
(CVA) with persistent defects (NIH < 4) associated with
ulcerative lesions and possible residual thrombus. In all
cases, the stenosis was crossed using a 0.014-in Sport wire
(Guidant-ACS, Inc.) and placed in the petrous portion of
the internal carotid artery. All stenoses were predilated with
a 4.0 × 20 mm Symmetry balloon (Medi-Tech, BSC, Inc.)
inflated to 8 atm for 5 s before placement of a 10 × 20 mm
Wallstent (Boston Scientific, Inc.). Postdilation was
completed with an appropriately sized balloon meeting a
balloon:artery ratio of 1:1 by visual estimate. Pan cerebral
angiography was performed before withdrawal of the Ar-
rowflex sheath from the common carotid artery.

A 6F femoral venous sheath was placed at the initiation of
the procedure for placement of a temporary pacemaker if
bradycardia was observed. Systolic arterial pressure was
maintained between 120 mm Hg to 160 mm Hg through-
out the procedure. All patients were admitted and observed
in the neurovascular intensive care for 24 h. The sheaths
were removed when the ACT was <170.

Carotid duplex scanning was performed within 24 h of
either procedure and at 1, 3, 6, 12 and 24 months and
expressed as the ratio of internal carotid artery/common
carotid artery velocity. Sequential neurologic examinations,
Rankin and Barthel scorings were performed concurrent
with Duplex scanning. Magnetic resonance imaging (MRI)
was obtained at 6 and 12 months to detect the presence of
asymptomatic ischemic events in the distribution of the
treated vessel (34).

Perception of pain was assessed in accordance with
guidelines commissioned by the Agency for Health Care
Policy and Research (35). No specific posthospitalization
instructions were provided in reference to activities; each
individual determined return to “full activity.”
Hospital variable costs included operating room or catheterization laboratory, nursing, pharmacy, laboratory and radiology. Professional charges were not assessed for stenting; hence, no physician’s fees were included in determination of any costs or charges. Costs/charges for the single fees were included in determining; hence, no physician’s.

Results are expressed as average ± SEM. Statistical comparisons were performed using Student t test. Two-way repeated measures of analysis of variance were used to compare sequential testing of carotid duplex scanning. A p value of <0.05 was considered statistically significant.

RESULTS

Demographics. The inclusion criteria, average ages and numbers of men and women of those randomized for CEA or CAS were similar (Table 1). The most common presenting event was a TIA. Those sustaining a CVA were functionally independent (NIH scores of <4 and Barthel Index >90). No patient experienced speech or comprehension dysfunction. Risk factors for stroke included hypertension, elevated cholesterol, smoking and diabetes. More than two risk factors were observed in more than 50% (70/104) of patients.

Results of treatment. Most patients (87/104) were treated within one month (range: 7 to 42 days) of the presenting symptom. All received definitive treatment by six weeks. Diagnostic cerebral angiography indicated the average pre-treatment stenosis in the CEA group (88.2 ± 13.2%) to be similar (p > 0.05) to the CAS group (82.4 ± 7.1%). The mean cross-sectional diameter as determined by the greatest stenosis observed on anteroposterior, lateral or oblique angiographic view was 1.6 ± 1.1 mm (range: 0.8 mm to 2.4 mm) in the CAS group and 1.7 ± 0.46 mm (range: 1.0 mm to 3.0 mm) in those undergoing CEA. The contralateral, asymptomatic carotid artery was found to have <50% stenosis in 70/104 patients, although total occlusion was observed in five and two individuals undergoing CAS or CEA, respectively. The average postangioplasty and stenting stenosis decreased to 5.0 ± 2.7% (range: 0% to 10%). The 24-month patency of the reconstructed artery remained satisfactory as determined by carotid ultrasound (Fig. 1). No MRI evidence of asymptomatic focal cerebral ischemia was found in any patient (data not shown).

Complications. No patient sustained a CVA, although one individual died from an immediate postoperative myocardial infarction subsequent to CEA (Table 2). This was the only procedurally related mortality experienced during this study. One patient experienced transient confusion associated with left sensory loss subsequent to postdilation of the stent that resolved within 10 min with elevation of the systolic blood pressure. Complications associated with CEA included wound hematoma requiring re-exploration (one patient) and peripheral nerve injury manifest as hoarseness (one patient) or lower facial and diminished sensations in the neck (three patients). These nerve injuries resolved within three months.

The most common occurrence associated with CAS was transient bradycardia (7/53) and/or hypotension (12/53) concurrent with angioplasty as a result of carotid body stimulation. None persisted more than 24 h. Initially, a

### Table 1. Baseline Characteristics of Study Patients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>CAS (n = 53)</th>
<th>CEA (n = 51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yrs)</td>
<td>66.4 (36–78)</td>
<td>69.6 (56–81)</td>
</tr>
<tr>
<td>Presenting symptom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke (NIH &lt; 4)</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Transient ischemia</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Amaurosis fugax</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>45</td>
<td>48</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Cholesterol (&gt;200)</td>
<td>34</td>
<td>24</td>
</tr>
<tr>
<td>Smoking</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>&gt;2 risk factors</td>
<td>38</td>
<td>32</td>
</tr>
<tr>
<td>Coronary vascular disease</td>
<td>39</td>
<td>31</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>27</td>
<td>31</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>48</td>
<td>48</td>
</tr>
</tbody>
</table>

CAS = carotid angioplasty and stenting; CEA = carotid endarterectomy.

### Table 2. Complications

<table>
<thead>
<tr>
<th>Category</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death/cerebral ischemia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Transient cerebral ischemia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial thrombosis/amputation</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hematomas requiring treatment</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Cranial/cervical nerve injury</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Bradycardia (temporary pacing)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Hypotension (requiring treatment)</td>
<td>12</td>
<td>3</td>
</tr>
</tbody>
</table>

CAS = carotid angioplasty and stenting; CEA = carotid endarterectomy.
temporary pacemaker was inserted prophylactically. However, in efforts to contain cost and due to infrequent use, this has been abandoned. Currently, severe and/or prolonged bradycardia and/or flux in blood pressure were treated pharmacologically. These events are anticipated and frequently resolve without treatment. Complications associated with CAS were contingent with femoral artery access similar to other routine interventional approaches used for coronary artery disease (36). Retroperitoneal hemorrhage occurred in the three patients who received the platelet IIb/IIIa receptor antibody, abciximab (ReoPro, Eli Lilly and Co., Indianapolis, Indiana) in conjunction with heparin. This complication can be avoided by adhering closely to recommendations for the use of heparin with this monoclonal antibody provided by the Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-term Outcome with Abciximab Glycoprotein IIa/IIIb Blockade (EPILOG) protocol (37). One individual with previously undiagnosed advanced generalized peripheral occlusive disease sustained popliteal artery thrombosis, which necessitated below-the-knee amputation. This was the only major complication in the CAS group.

Length of hospital stay. The length of hospitalization was similar for both groups, although those undergoing CAS without complication tended to be discharged sooner (Table 3). As the study progressed, patients in the CEA group remained in the hospital for shorter periods, most being discharged the day after surgery. Forty-four patients (44/53) in the CAS group (83%) and 34 patients (34/51) in the CEA group (67%) were discharged from the hospital the day after the procedure. Excluding the single patient requiring below-the-knee amputation whose hospitalization extended to 68 days, overall hospital stays tended to be shorter in the CAS group (2.6 ± 1.6 days vs. 3.7 ± 3.1 days). Nevertheless, complications prolonged hospital care slightly more in the CAS group (5.6 ± 3.7 days vs. 3.8 ± 3.5 days). The primary complication associated with CAS was related to femoral artery access (3/53), which prolonged hospitalization because of continued bed rest and/or transfusion. Cranial/peripheral nerve injuries associated with CEA (4/51) did not prolong hospitalization. Hospitalization was extended secondary to concurrent or subsequent coronary bypass surgery in five patients. This procedure added an average of 10 ± 2 days to hospitalization. Neither CAS nor CEA afforded an advantage in terms of shortened stay in this small group of patients.

Patient's perception of pain and return to activity. The perception of pain was similar in both groups; neither experienced pain beyond a rating of 5/10 (Table 4). Most symptoms resolved by one month. Return to full activity was achieved within one week by 43 of the 53 patients undergoing CAS and 34 of the 51 patients randomized to CEA. All individuals in the CEA group resumed full activity by one month. However, complications in the CAS group significantly prolonged convalescence (57 to 120 days).

Cost/charges. Variable costs reflect the actual expenditures of performing a specific procedure, thus provide an accurate accounting of CEA and CAS. The total variable costs associated with CAS and CEA are similar (p = 0.89) (Table 5). As anticipated, individual hospital costs and charges resulting from the occurrence of complications varied widely, although they were higher for the CAS group secondary to prolonged hospitalization. Charges to patients, which did not include any professional fees, were higher in the CEA group (p = 0.01).

DISCUSSION

Endovascular technology has advanced to include treatment of carotid occlusive disease (23,24,26–29,38). Although proponents suggest that stenting may be effective in reducing carotid stenosis, its use has been recommended without testing its “clinical equipoise” (39) against the standard of care, endarterectomy. The single published randomized study designed to address this issue was suspended because of significant numbers of disabling strokes associated with

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**Table 3. Days Length of Hospital Stay***

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>5.2 ± 11.4 days (1–68)†</td>
<td>3.7 ± 3.1 days (1–14)</td>
</tr>
<tr>
<td>Without complications</td>
<td>1.8 ± 0.58 days (1–4)</td>
<td>2.7 ± 1.2 days (1–13)</td>
</tr>
<tr>
<td>With complications</td>
<td>13.3 ± 21 days (3–68)†</td>
<td>3.8 ± 3.5 days (1–14)</td>
</tr>
</tbody>
</table>

*Avg ± SEM (range); †Exempting the single patient with major vascular complication, overall length of stay for CAS = 2.6 ± 1.6 days. Average length of stay for patients undergoing CAS who experienced other complications = 5.6 ± 3.7 days (3–11).

CAS = carotid angioplasty and stenting; CEA = carotid endarterectomy.

**Table 4. Perception of Perioperative Pain and Activity**

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain scale (0–10)</td>
<td>1.2 (range 0–5)</td>
<td>2.7 (range 0–5)</td>
</tr>
<tr>
<td>24 h postprocedure (avg)</td>
<td>&lt;1.0 (0–4)</td>
<td>&lt;1.0 (0–4)</td>
</tr>
<tr>
<td>1 month postprocedure</td>
<td>12 days (2–30)</td>
<td>16 days (7–30)</td>
</tr>
<tr>
<td>Return to full activity (average days)</td>
<td>120 days (57–140)</td>
<td>21 days (9–30)</td>
</tr>
</tbody>
</table>

Without complication

Without complications

CAS = carotid angioplasty and stenting; CEA = carotid endarterectomy.
stenting (32). Other multicenter prospective, randomized trials comparing CAS with CEA have been suspended (40) or have yet to be initiated (41). This report presents initial observations of a clinical trial designed to investigate the safety and effectiveness of carotid stenting compared with CEA in treating symptomatic carotid occlusive disease in a community hospital.

Equipoise of stenting and endarterectomy. Our results agree that carotid stenting is equally as effective as CEA in correcting and maintaining postprocedure patency of carotid stenosis (24,26,28,42). Equipoise is further supported by MRI, indicating that no asymptomatic ischemic events occurred in the distribution of the treated vessel subsequent to either revascularization technique (data not shown). The occurrence of major or minor stroke or death associated with CAS or CEA was well within the limits of acceptable risk delineated by the NASCET (1,4) and Asymptomatic Carotid Arteriosclerosis study (43) yet markedly differed from previous reports of nonrandom series indicating a risk for major or minor stroke associated with CAS approaching 6% (31). Although the “learning curve” for CAS is about 50 cases (31,42), the occurrence rates for serious complications in series involving an excess of 100 patients is higher than those associated with CEA (26,28,31,43,44). The low number of neurologic complications observed in this trial reflects a “cerebral endovascular team” comprised of neurosurgeons possessing skills in endarterectomy and catheter-based techniques, experienced interventional cardiologists and neurologists.

Economic issues of carotid stenting versus endarterectomy. Economic evaluation of stroke prevention and treatment is an important factor in the health care sector (45–47). Thus, the deference toward evidence-based medicine now includes a demand for “cost-effectiveness” of new and existing technologies. This trial addresses these issues as characterized by length of hospital stay, the return to full activity, patient’s perception of pain associated with the procedure and hospital costs. The occurrence of major or minor stroke was not observed in this trial regardless of the revascularization procedure. Thus, in contradistinction to Jordan et al. (31), these cerebrovascular complications cannot be deployed in an economic argument favoring CEA over CAS. Initially, stenting resulted in a shortened hospital stay with most patients being discharged within 24 h. However, based on our experience and that of others, that complications associated with endarterectomy occur within 6 h, a growing tendency toward shorter hospitalization after CEA has evolved (48–50). Most patients undergoing CEA are discharged within 24 h. Although, the theoretical advantage of “early” hospital discharge supposed through percutaneous technology has yet to be determined, hospital stay subsequent to CAS may be lessened in the future through miniaturization of technology and routine use of arterial closure devices.

As expected, hospitalization is prolonged by procedural complications. Cranial or peripheral nerve injury or neck hematomas that are rapidly recognized and appropriately treated do not influence hospital stay (1,16); however, the occurrence of clinically significant retroperitoneal hemorrhage does prolong hospitalization (36). Although anticoagulation is necessary, the paradigm used in stenting probably can be lessened because most cerebral ischemic events are associated with post-stent dilation, at which time atheromatous material may be released from the arterial wall rather than hematologic emboli (51). Routine use of distal protection devices in conjunction with less anticoagulation may reduce the risk of both excessive retroperitoneal and intraprocedural ischemic events. However, the addition of distal protection devices designed to prevent cerebral embolization of atheromatous material actually may increase cost/charges.

The evaluation of pain and return to full activity also judges the economic efficiency of a procedure. The frequent bias that “open” surgical techniques are less well tolerated in terms of pain and discomfort than percutaneous approaches is not supported by this trial. Both procedures seem equally well tolerated in terms of pain and discomfort. Moreover, return to full activity was achieved in about two weeks regardless of the procedure. However, return to full activity was delayed by complications particularly after CAS. Pain associated with groin complications is more limiting than those involving incisions in the neck in terms of active daily living.

Whereas, this study shows that the effectiveness of CAS is equivalent to CEA in terms of the ability to correct symptomatic carotid stenosis without increased risk for major or minor stroke, fiscal considerations tend to favor CEA (52). Although pharmacy and “routine” hospital costs and charges may be similar, expenditures associated specifically with cardiac catheterization laboratories compared with standard operating rooms are higher. Stents, angioplasty balloons, catheters, guiding wires, sheaths and the use of temporary pacemakers are costly and nonreusable. If the use of a distal protection device becomes a “standard of care,” the costs will escalate further. These data suggest that, from a perspective of an economic evaluation, the potential

### Table 5. Comparison of Variable Costs/Patient Charges

<table>
<thead>
<tr>
<th></th>
<th>Total Costs</th>
<th>Nursing Costs</th>
<th>Cath/OR Lab</th>
<th>Pharmacy Costs</th>
<th>Lab Costs</th>
<th>Radiology Costs</th>
<th>Charges (Excluding Doctor Fees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS</td>
<td>4,077 ± 460</td>
<td>327 ± 39</td>
<td>3,550 ± 286</td>
<td>66 ± 16</td>
<td>81 ± 26</td>
<td>105 ± 11</td>
<td>6,653 ± 367</td>
</tr>
<tr>
<td>CEA</td>
<td>3,415 ± 1,289</td>
<td>1,187 ± 101</td>
<td>1,159 ± 359</td>
<td>470 ± 229</td>
<td>79 ± 41</td>
<td>108 ± 58</td>
<td>5,594 ± 166</td>
</tr>
</tbody>
</table>

*Expressed as Avg ± SEM.
CAS = carotid angioplasty and stenting; CEA = carotid endarterectomy; OR = operating room.
effect gained through percutaneous carotid stenting may be lessened by increased incremental cost/charges.

**Study limitations.** This trial is limited to a single institution, and a select “team” with experience in cerebral vascular disease and endovascular techniques, thus, cannot advocate that CAS replace CEA as a primary revascularization procedure in patients with symptomatic carotid stenosis. However, it is the first randomized prospective study to demonstrate that carotid angioplasty and stenting is equivalent to endarterectomy for the treatment of symptomatic carotid stenosis without added risk for major or minor stroke. If the economic constraints of incremental costs associated with stenting can be overcome, this trial indicates that CAS has reached clinical equipoise with CEA.

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**REFERENCES**