Carotid artery angioplasty with stenting and postprocedure hypotension

Brian Park, M.D. a, David Shapiro, M.D. a, Michael Dahn, M.D., PhD. a,*, Melih Arici, M.D. b

a Department of Surgery, University of Connecticut, 263 Farmington Avenue, MC3955, Farmington, CT 06030-3955, USA
b Department of Radiology, University of Connecticut, Farmington, CT, USA

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Abstract

Introduction: Although carotid endarterectomy (CEA) has become established as the preferred approach to the management of critical carotid stenosis, carotid angioplasty with stenting (CAS) has arisen as a competitive modality. We report here a nonindustry-supported experience using CAS in a nonselected patient population suffering from critical carotid stenosis.

Methods: All patients suffering from carotid stenosis (>50% symptomatic or >80% asymptomatic) were offered CAS or CEA. The first 36 patients who underwent attempted CAS over this last year are reported here. CAS was performed with the SMART PRECISE (Cordis, Inc, Miami Lakes, FL) or ACCULINK (Guidant, Inc, St Paul, MN) stents. All procedures were performed with cerebral protection.

Results: The planned procedure success rate was 97%, and the major adverse event (MAE) rate was 3.0% in 35 patients who underwent successful CAS. This included a minor stroke and a subendocardial myocardial infarction in the same individual. Both events were attributed to sustained postprocedure hypotension. The most frequent intraprocedure complications observed were bradycardia and hypotension. Persistent postprocedure hypotension requiring vasopressor support complicated 23% of cases. The average duration of vasopressor support in this group was 21 hours.

Conclusion: CAS can be accomplished with an MAE comparable to CEA and will likely become the dominant alternative to CEA for the management of carotid stenosis. Management of periprocedural cardiovascular instability represents one of the most important elements in the safe conduct of CAS. © 2005 Excerpta Medica Inc. All rights reserved.

Keywords: Carotid angioplasty; Stenting; Cerebral protection; Hypotension; Stroke; Endarterectomy

Cerebrovascular disease is the third leading cause of death in the United States [1]. It is associated with 700,000 strokes per year, resulting in a huge morbidity and economic burden to our society. Approximately 20% to 35% of these strokes are attributable to extracranial carotid occlusive disease [2]. Consequently, clinical management of carotid stenosis has been intensively studied for decades. Currently, carotid endarterectomy (CEA) is the primary modality used to treat asymptomatic and symptomatic carotid stenosis. The efficacy of CEA in the management of carotid stenosis has been proven and its durability reaffirmed through prospective trials including the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [3], Asymptomatic Carotid Atherosclerosis Study (ACAS) [4], European Carotid Surgery Trial (ECST) [5], and Asymptomatic Carotid Surgery Trial (ACST) [6]. For example, the NASCET trial has shown that the 2-year ipsilateral stroke risk for symptomatic occlusive disease in the stenosis range of 70% to 99% range is 9% for patients undergoing CEA and 26% for patients undergoing the best medical therapy. Furthermore, 30-day adverse events such as stroke, myocardial infarction, and death associated with each respective approach were similar (5.8% for endarterectomy and 3.3% for best medical management).

In contrast, the observed morbidity and mortality rates for the application of carotid angioplasty to seriously ill patients had been reported to be in the range of 12% to 33% [7,8]. Counsell et al [9] reported the early termination of a randomized trial comparing CEA with angioplasty because 5 of the first 7 patients entered into the angioplasty arm suffered a stroke, suggesting that this procedure was associated with excessive risk. Finally, Golledge et al [10] reported that the risk of stroke and death associated with

* Corresponding author. Tel.: +1-860-679-4801; fax: +1-860-679-1276. E-mail address: dahn@uchc.edu

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Angioplasty indications

Duplex peak velocity of target internal carotid artery* 311 cm/s (Guidant, Inc) cerebral protection device. After placement either the Filter Wire (Boston Scientific, Inc) or ACCUNET ACCULINK (Guidant, Inc) stents, and all procedures used performed by using the SMART Precise (Cordis, Inc) or section of the radiology department. Carotid stenting was formed under conscious sedation in the special procedures (aspirin) for 5 days before the procedure. CAS was per-

Sanofi-Aventis, Bridgewater, NJ) and acetylsalicylic acid col. All patients were pretreated with clopidogrel (Plavix; from an industrial sponsor.

CAS versus CEA[11]. The present report received no funds randomized, prospective trial evaluating the efficacy of in the SAPPHIRE trial, which is an industry-supported, made them comparable to the patients reported previously these patients exhibited numerous comorbid factors, which to the anatomic criteria used for CEA. This includes an to study angioplasty and carotid artery stenting (CAS). This has resulted in a variety of refinements, which have been applied to this procedure to make it a realistic alternative to surgical management of carotid artery stenosis.

Methods and Materials

All potential candidates for carotid artery reconstruction were offered either CEA or CAS, and the patients were permitted to express their preference. In this article, we will report the results of our first 36 consecutive patients who accepted CAS.

Criteria for acceptance of patients for CAS were identi-
cal to the anatomic criteria used for CEA. This includes an internal carotid artery stenosis of 80% for asymptomatic and 50% stenosis for symptomatic patients. The majority of these patients exhibited numerous comorbid factors, which made them comparable to the patients reported previously in the SAPPHIRE trial, which is an industry-supported, randomized, prospective trial evaluating the efficacy of CAS versus CEA [11]. The present report received no funds from an industrial sponsor.

Briefly, the conduct of CAS followed a standard proto-
col. All patients were pretreated with clopidogrel (Plavix; Sanofi-Aventis, Bridgewater, NJ) and acetylsalicylic acid (aspirin) for 5 days before the procedure. CAS was performed under conscious sedation in the special procedures section of the radiology department. Carotid stenting was performed by using the SMART Precise (Cordis, Inc) or ACCULINK (Guidant, Inc) stents, and all procedures used either the Filter Wire (Boston Scientific, Inc) or ACCUNET (Guidant, Inc) cerebral protection device. After placement of the cerebral protection device, patients underwent predi-
latation of the carotid stenosis with a 4-mm balloon. All patients received 0.5 mg of atropine before balloon angioplasty to minimize bradycardia. Additionally, after stent deployment, all patients received an additional 0.5 mg of atropine before final stent dilatation. The occurrence of subsequent hypotension was controlled by the initiation of dopamine infusion, which was titrated to a systolic blood pressure >110 mmHg and <180 mmHg. The patients remained in the intensive care unit until dopamine could be discontinued.

After the procedure, patients were maintained on clo-
pidrogel (Plavix) for 6 weeks. Duplex surveillance was begun at 6 weeks postprocedure and continued every 6 months thereafter for a 2-year period. Average data are provided as population means ± standard deviation.

Results

Of the 36 patients who underwent CAS, 35 had a suc-
cessful procedure. The patient characteristics are indicated on Table 1. The extent of the carotid disease is indicated by the average internal carotid artery peak systolic velocity on duplex scan, which was 311 ± 76 cm/s. One patient underwent predilatation of the internal carotid artery followed by stent deployment, but the internal carotid artery could not be dilated to a satisfactory luminal diameter because of a recalcitrant stenosis from a prior CEA. This patient underwent open surgical reconstruction of this vessel with stent ex-
plantation and is considered an unsuccessful procedure. The remaining 35 patients form the basis of this report. Of these 35 patients, all subjects underwent angioplasty with CAS.

One patient suffered an ipsilateral stroke of the internal capsule (modified Rankin Stroke Scale 2) in conjunction with a myocardial infarction. This occurred in association with a protracted period of hypotension after internal carotid artery dilation, suggesting that the etiology of this series of events was blood pressure related. The neurologic symp-
toms of weakness in this patient resolved after 3 days. Consequently, the 30-day stroke rate for this series was 3.0%. These results are summarized in Table 2.

Significant postprocedural hypotension occurred in 8 of the 35 patients who underwent CAS stenting (23%). Sig-
nificant hypotension was defined as a greater than 40 mm

<table>
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<th>Table 1</th>
<th>Study patient characteristics (n = 36)</th>
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<td>Patient characteristics</td>
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<tr>
<td>Average patient age</td>
<td>70 ± 11 years</td>
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<td>Duplex peak velocity of target internal carotid artery*</td>
<td>311 ± 76 cm/s</td>
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<td>Angioplasty indications</td>
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<tr>
<td>Asymptomatic</td>
<td>25 (70%)</td>
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<tr>
<td>Transient ischemic attack</td>
<td>4 (12%)</td>
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<tr>
<td>Previous hemispheric stroke</td>
<td>4 (12%)</td>
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<tr>
<td>Nonhemispheric symptoms</td>
<td>2 (6%)</td>
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* Upper limit of normal, PSV = 110 cm/s.

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<tr>
<th>Table 2</th>
<th>Results of carotid angioplasty with stenting (n = 36)</th>
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<td>Results</td>
<td>Occurrences (%)</td>
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<tr>
<td>Successful procedures</td>
<td>35 (97)</td>
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<td>Common carotid procedures</td>
<td>2 (6)</td>
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<tr>
<td>Procedure-related mortalities</td>
<td>0</td>
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<tr>
<td>Non–procedure-related mortalities</td>
<td>0</td>
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<tr>
<td>Major adverse events (strokes, myocardial infarction, death)</td>
<td>1 (3)</td>
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The current guidelines for the management of carotid stenosis as prophylaxis against stroke are currently well defined. The efficacy of surgical management for carotid stenosis has been proven using evidence-based medicine through the NASCET [3], ACAS [4], ECST [5] trials, and so on. These randomized, prospective clinical trials have proven the utility of CEA in stroke prevention in patients who exhibit moderate to severe stenosis of the origin of the internal carotid artery. Additionally, as mentioned previously, early studies of carotid angioplasty have been associated with a higher procedural stroke risk when compared with CEA. Thus, it would suggest that the minimally invasive approach of carotid angioplasty remains substantially inferior to surgical therapy for this disease entity. However, in recent years, clinical trials have suggested the equivalency of carotid angioplasty with CEA as a consequence to refinements in the technique of carotid angioplasty [12]. The SAPPHIRE trial has received the greatest attention in this regard [11]. This was an industry-sponsored (Cordis, Inc), randomized, prospective trial evaluating high-risk patients exhibiting carotid stenosis randomized to either carotid angioplasty with stent placement (CAS) or CEA. The outcome of this trial revealed a statistical benefit in the major adverse event rate (combined death, stroke, and myocardial infarction rate) favoring CAS (5.8%) when compared with CEA (12.6%) at 30 days. A number of additional single-arm trials have reported comparable major adverse event rates to the SAPPHIRE stenting arm. Although these additional trials show results consistent with SAPPHIRE, these studies rely on historical surgical data with no concurrent comparators. The Carotid Revascularization Using Endarterectomy or Stenting Systems (CARESS) trial, which was funded by the International Society of Endovascular Specialists, was a randomized trial, which did include CEA endarterectomy as a comparator arm [13]. This study showed that there was no significant difference in the 30-day combined all-cause mortality and stroke rate between CEA (2%) and CAS (2%). This report concluded that the 30-day risk of stroke or death after CAS with cerebral protection is equivalent to CEA. A recent update of this trial has indicated that there was no significant difference in the 1-year combined all-cause mortality and stroke rate between CEA (13.6%) and CAS (10.0%). Significantly, the CARESS trial included a patient population that was not limited to high-risk patients, indicative of the trend in this field of including all patients as candidates for carotid artery angioplasty and stenting. This was the strategy used in the current study. The patient population reported here is unsolicited with respect to risk or symptomatology, yet is representative of the patient population at risk for stroke. The mean age of the patients was 70 years of age, and the patients exhibited high-grade disease as evidenced by an average duplex peak systolic velocity of 311 cm/s in the target internal carotid artery (Table 1).

The current study findings are consistent with recent reports indicating the CAS can be accomplished with a low rate of adverse events. The observed major event rate in this study was 3.0%, which resulted from a single case of minor stroke and no deaths. We attribute this low complication rate to several factors including careful attention to preprocedure antiplatelet therapy, meticulous attention to procedure protocol, and routine use of cerebral protection devices. This latter factor has been associated with a reduction of the periprocedure stroke rate by 50% compared with unprotected procedures when applied routinely [14].

Several questions remain regarding the utility of the carotid angioplasty and stenting as a potential competitor or replacement therapy for CEA. The cost analysis of CAS has not been reported to date and may significantly influence the acceptability of this procedure. Currently, the major high-end cost factors involved in the stenting procedure include dedicated self-expanding nitinol stents costing $2,000 to $2,500 per stent. This represents a doubling in the cost of nondedicated nitinol stents used for peripheral vascular indications. At the time of this writing, one device (ACCULINK) has been approved specifically for carotid indications by the Food and Drug Administration. It is likely that several additional devices will receive a similar indication within the next 6 months, which may decrease the material costs of this procedure. Furthermore, the standard of care in this area requires the use of cerebral protection. This most commonly involves the use of filtration devices that are temporarily deployed in the distal internal carotid artery during the conduct of the procedure in an effort to minimize cerebral embolization during the procedure. The ACCUNET device, manufactured by Guidant, Inc, has received Food and Drug Administration approval specifically for this application. The cost of this device ranges between $1,500 and $2,000.

### Table 3

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<tr>
<th>Incidence of significant hypotension and bradycardia postprocedure*</th>
<th>Occurrences (%)</th>
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<tr>
<td>Hypotension requiring intravenous pressors</td>
<td>8 (23)</td>
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<tr>
<td>Bradycardia requiring transvenous pacing</td>
<td>0</td>
</tr>
<tr>
<td>Bradycardia requiring transtunaneous pacing</td>
<td>0</td>
</tr>
<tr>
<td>Mean duration of pressor support</td>
<td>21 hours (range 12 to 36 hours)</td>
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* Significant hypotension was defined as a decrease in systolic blood pressure by 40 mm Hg or a systolic blood pressure less than 90 mm Hg.

Hg drop in blood pressure or a systolic blood pressure less than 90 mm Hg. These patients required intravenous vasoressor support during their stay in the intensive care unit. The mean duration of pressor support was 21 hours (range, 12 to 36 hours). However, none of our patients required either transtunaneous or transvenous temporary pacing for persistent bradycardia. These results are summarized in Table 3.

### Comments

The current guidelines for the management of carotid stenosis as prophylaxis against stroke are currently well defined. The efficacy of surgical management for carotid stenosis has been proven using evidence-based medicine through the NASCET [3], ACAS [4], ECST [5] trials, and so on. These randomized, prospective clinical trials have proven the utility of CEA in stroke prevention in patients who exhibit moderate to severe stenosis of the origin of the internal carotid artery. Additionally, as mentioned previously, early studies of carotid angioplasty have been associated with a higher procedural stroke risk when compared with CEA. Thus, it would suggest that the minimally invasive approach of carotid angioplasty remains substantially inferior to surgical therapy for this disease entity. However, in recent years, clinical trials have suggested the equivalency of carotid angioplasty with CEA as a consequence to refinements in the technique of carotid angioplasty [12]. The SAPPHIRE trial has received the greatest attention in this regard [11]. This was an industry-sponsored (Cordis, Inc), randomized, prospective trial evaluating high-risk patients exhibiting carotid stenosis randomized to either carotid angioplasty with stent placement (CAS) or CEA. The outcome of this trial revealed a statistical benefit in the major adverse event rate (combined death, stroke, and myocardial infarction rate) favoring CAS (5.8%) when compared with CEA (12.6%) at 30 days. A number of additional single-arm trials have reported comparable major adverse event rates to the SAPPHIRE stenting arm. Although these additional trials show results consistent with SAPPHIRE, these studies rely on historical surgical data with no concurrent comparators. The Carotid Revascularization Using Endarterectomy or Stenting Systems (CARESS) trial, which was funded by the International Society of Endovascular Specialists, was a randomized trial, which did include CEA endarterectomy as a comparator arm [13]. This study showed that there was no significant difference in the 30-day combined all-cause mortality and stroke rate between CEA (2%) and CAS (2%). This report concluded that the 30-day risk of stroke or death after CAS with cerebral protection is equivalent to CEA. A recent update of this trial has indicated that there was no significant difference in the 1-year combined all-cause mortality and stroke rate between CEA (13.6%) and CAS (10.0%). Significantly, the CARESS trial included a patient population that was not limited to high-risk patients, indicative of the trend in this field of including all patients as candidates for carotid artery angioplasty and stenting. This was the strategy used in the current study. The patient population reported here is unsolicited with respect to risk or symptomatology, yet is representative of the patient population at risk for stroke. The mean age of the patients was 70 years of age, and the patients exhibited high-grade disease as evidenced by an average duplex peak systolic velocity of 311 cm/s in the target internal carotid artery (Table 1).

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Thus, the addition of these 2 devices to the management of carotid stenosis will substantially alter the cost of a therapeutic carotid intervention, which is currently one of the most commonly performed vascular interventions in the United States today.

A second issue revolves around the durability of angioplasty in relationship to CEA. Currently, long-term studies assessing the degree of restenosis after intervention remain scant. Lal et al [15] has recently reported that the restenosis rate for carotid angioplasty is 6.4% at 60 months, which is comparable to the restenosis rate of CEA. However, additional long-term data will be required to fully assess this aspect of this procedure.

A third issue raised in this study is the high incidence of postprocedure hypotension observed after carotid stenting. This phenomenon is significantly higher than that seen with CEA and has been noted by several authors [17–21]. A recent literature review on this subject reported the incidence of hypotension and bradycardia ranging from 29% to 51% [18]. Postprocedure hypotension in this particular patient population has been associated with a greater incidence of increased complications, poor long-term prognosis, and death [21]. Many theorize that this phenomenon occurs because of excessive stretching of the baroreceptors in the carotid bulb by the angioplasty and stenting procedures [18]. Dangas et al [21] observed, “... there is an important association between post-CAS hypotension and procedural factors that might lead to more aggressive carotid sinus stretching. The endovascular deployment of balloon-expandable stents with larger final balloons rather than self-expanding stents was associated with the development of post-CAS hypotension.” Their data did indicate that a greater incidence of hypotension is associated with balloon-expandable stents versus self-expanding stents (34% versus 14%) [21]. The occurrence of significant hypotension in our patients required intravenous pressor support, which frequently extended the intensive care unit and hospital stay. Although some groups have advocated prophylactic administration of atropine before angioplasty [19] or even temporary tranvenous pacemakers [20], no clinical trials have been performed to date to evaluate the efficacy of these modalities.

The diminished cardiovascular reserve and the comorbidities inherent to this particular patient population mandate that efforts be made to optimize their hemodynamic status preprocedure, intraprocedure, and postprocedure. Usually, these patients are nil per os after midnight before the procedure, resulting in a significantly dehydrated state. This might require intravenous fluid resuscitation before and during the procedure, although this contributes risk in patients who exhibit a high incidence of coronary artery disease. Nonetheless, a simple modification of our current preprocedural protocol would be to instruct our patients to consume an ounce of water every hour up to midnight the night before surgery. This simple intervention would reduce a significant amount of periprocedural fluid resuscitation. In addition, the patients of this population often take multiple antihypertensive medications. We currently recommend that these patients take their antihypertensive medications during the morning of surgery. This current practice must be reexplored and particularly potent medications in terms of those that affect hemodynamic status should be temporarily discontinued.

During the angioplasty, because manipulation of the carotid bulb by the angioplasty balloon seems to be strongly associated with hypotension and bradycardia, attempts to minimize this manipulation may also reduce the incidence of periprocedural and postprocedural hypotension [18]. Efforts to explore the effect of reducing both the frequency and duration of angioplasty balloon dilation of the carotids in terms of postprocedure hypotension may prove beneficial. Our current protocol includes 2 doses of intravenous atropine during key points in the procedure. Both the safety and efficacy of prophylactic dosing of atropine during carotid angioplasty and stenting need to be fully explored. A final technical point involves the immediate availability of pressor agents for these patients. In our institution, our current protocol for carotid angioplasty and stenting requires the immediate availability of premixed pressor agents in the interventional suite dedicated for these patients. The relatively high incidence of postprocedural hypotension as seen in our study and other studies justifies the added cost of dedicated, premixed pressor medications for these patients. The results of our study and that of other groups indicate a necessity to explore and clarify the management and prophylactic measures for postprocedural hypotension.

At the present time, the center for Medicare services has approved this procedure for reimbursement, although specific inclusion criteria remain incompletely defined [16]. Consequently, numerous educational facilities are now offering training programs in carotid angioplasty, and it is expected that there will be a major shift in the management of carotid stenosis. Currently, approximately 120,000 CEAs are performed annually in the United States. In view of the greater applicability of this procedure to high-risk patients, it appears likely that the volume of carotid angioplasties will eventually exceed this number if this procedure is fully embraced by the medical community.

References


