

# Stroke

American Stroke  
Association<sup>SM</sup>

JOURNAL OF THE AMERICAN HEART ASSOCIATION

A Division of American  
Heart Association



**Effect of Treatment of Carotid Artery Stenosis on Blood Pressure: A  
Comparison of Hemodynamic Disturbances After Carotid Endarterectomy and  
Endovascular Treatment**

F.M. McKeivitt, A. Sivaguru, G.S. Venables, T.J. Cleveland, P.A. Gaines, J.D. Beard  
and K.S. Channer

*Stroke* 2003;34;2576-2581; originally published online Oct 30, 2003;

DOI: 10.1161/01.STR.0000097490.88015.3A

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214  
Copyright © 2003 American Heart Association. All rights reserved. Print ISSN: 0039-2499. Online  
ISSN: 1524-4628

The online version of this article, along with updated information and services, is  
located on the World Wide Web at:

<http://stroke.ahajournals.org/cgi/content/full/34/11/2576>

Subscriptions: Information about subscribing to Stroke is online at  
<http://stroke.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters  
Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax:  
410-528-8550. E-mail:  
[journalpermissions@lww.com](mailto:journalpermissions@lww.com)

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

# Effect of Treatment of Carotid Artery Stenosis on Blood Pressure

## A Comparison of Hemodynamic Disturbances After Carotid Endarterectomy and Endovascular Treatment

F.M. McKeivitt, MRCP; A. Sivaguru, MRCP, MD; G.S. Venables, DM, FRCP;  
T.J. Cleveland, FRCS, FRCR; P.A. Gaines, FRCP, FRCR;  
J.D. Beard, ChM, FRCS; K.S. Channer, MD, FRCP

**Background and Purpose**—Carotid intervention by carotid endarterectomy (CEA) or endovascular treatment may cause hemodynamic change. The immediate and long-term effects on blood pressure after these procedures were assessed.

**Methods**—Patients were randomized to CEA (n=49) or endovascular treatment (n=55) that comprised percutaneous transluminal angioplasty alone (n=31), balloon-expandable stent (n=13), or self-expandable stent (n=11). A baseline 24-hour ambulatory blood pressure recording was made before carotid intervention and repeated at 24 hours, 1 month, and 6 months after the procedure.

**Results**—In the first 24 hours after the procedure, episodes of hypotension occurred in 75% of the CEA group and 76% of the endovascular group; hypertension occurred in 11% and 13%, respectively. There was a significant fall in blood pressure at 1 hour after the procedure in both groups (24 and 16 mm Hg fall in CEA and endovascular groups, respectively), but this was only sustained in the endovascular group. The pattern of blood pressure response in the first 24 hours was significantly different ( $P<0.0001$ , ANCOVA). Systolic blood pressure was significantly lower at 1 and 6 months only in the surgical group (6 and 5 mm Hg fall, respectively).

**Conclusions**—Both CEA and endovascular treatment have an effect on blood pressure stability, particularly within the first 24 hours after the procedure. (*Stroke*. 2003;34:2576-2582.)

**Key Words:** angioplasty, balloon ■ blood pressure ■ carotid endarterectomy ■ carotid stenosis

Acute hemodynamic instability after carotid endarterectomy (CEA) is a well-recognized phenomenon.<sup>1,2</sup> Both hypotension and hypertension can occur and may result in prolonged hospital admission or, more seriously, may be associated with neurological complications.<sup>3</sup> Close monitoring in the postoperative period is required for early recognition and correction of these hemodynamic disturbances. Carotid angioplasty and stenting (endovascular treatment) has become a popular alternative to CEA. No differences in postoperative stroke and mortality rates were noted in the 2 completed randomized controlled trials comparing these techniques.<sup>4,5</sup> Endovascular treatment is performed under local anesthetic, enabling treatment of high-risk surgical patients, and avoids other potential surgical complications, including cranial nerve injury and neck hematoma.<sup>4</sup> Fluctuations in blood pressure after endovascular treatment have been reported,<sup>6-8</sup> but the frequency has not been compared with that after CEA.

### See Editorial Comment, page 2581

This is the first study to compare the effect of both CEA and endovascular treatment on blood pressure within the first 6 months after treatment and the first to assess the longer-term effects of endovascular treatment on blood pressure.

### Subjects and Methods

Patients randomized into the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS), a multicenter, randomized trial to investigate the risks and benefits of surgical versus endovascular intervention for symptomatic carotid stenosis, were consecutively invited to participate from 1 CAVATAS center. Separate written consent was obtained from each patient for inclusion into this additional study, and approval was obtained by the local ethics committee and the CAVATAS management committee. During the study period, 49 patients were randomized to CEA and 55 to endovascular treatment, which comprised percutaneous transluminal angioplasty (PTA) alone (n=31), PTA with a balloon-expandable stent (n=13), or PTA with a self-expandable stent (the currently

Received December 3, 2002; final revision received July 16, 2003; accepted July 16, 2003.

From the Departments of Neurology (F.M.M., A.S., G.S.V.) and Cardiology (K.S.C.), Royal Hallamshire Hospital, and Sheffield Vascular Institute, Northern General Hospital (T.J.C., P.A.G., J.D.B.), Sheffield Teaching Hospitals National Health Service Trust, Sheffield, UK.

Reprint requests to Dr Fiona McKeivitt, Department of Neurology, Royal Hallamshire Hospital, Glossop Rd, Sheffield S10 2JF, UK. E-mail fionamckeivitt@hotmail.com

© 2003 American Heart Association, Inc.

*Stroke* is available at <http://www.strokeaha.org>

DOI: 10.1161/01.STR.0000097490.88015.3A

accepted technique) (n=11). A prospective observation of the effects on blood pressure was performed.

### Carotid Endarterectomy

All patients underwent a standardized general anesthetic for the duration of the study period. Diazepam 10 mg was used as a premedication, with midazolam (2 to 3 mg), etomidate (10 to 20 mg), and alfentanil (2.5 mg) used as induction agents. Vecuronium (10 mg) was used for neuromuscular blockade. Nitric oxide, oxygen, and isoflurane were used during maintenance of general anesthesia. The surgical technique was also standardized. The carotid sinus nerve was preserved and injected with lidocaine before carotid artery clamping. Shunting and Dacron patch angioplasty were performed routinely. Patients were then transferred to a high-dependency unit for 24 hours after the procedure. Blood pressure was maintained at  $\pm 30$  mm Hg of the preprocedure systolic blood pressure, with the use of esmolol as a hypotensive agent (to reduce the risk of hyperperfusion injury<sup>9</sup>) or phenylephrine as a hypertensive agent if required.

### Carotid Angioplasty and Stent

After selective angiography of the femoral artery was performed, a 7F long sheath or 9F guiding catheter was passed into the common carotid artery. Intra-arterial atropine (1.2 mg) was given, and the lesion was crossed with a V18 control wire (Boston Scientific). If balloon angioplasty was used, the balloon size was selected after measurement of the internal carotid artery. If the result was considered insufficient, a stent was placed (secondary stenting). During the study period, routine use of stents with prior 3 mm predilatation became the strategy (primary stenting). Postdilatation of the stent was routine, with the use of a balloon compatible with the internal carotid artery above the stenosis. Both balloon-expandable stents (Palma-Schatz, Cordis) and self-expanding stents (Wallstent, Schneider) were used.

An intravenous heparin bolus of 5000 U was given during the procedure and then continued as an intravenous infusion for 24 hours to achieve an activated partial thromboplastin time ratio of 1.5 to 2.5. Patients were then transferred back to the neurology ward for observation. No active management of blood pressure by esmolol or phenylephrine was used.

In addition to the CAVATAS protocol,<sup>4</sup> a previously validated 24-hour ambulatory blood pressure recording (Space Labs SL-90207) was taken, before carotid intervention, to obtain a mean baseline systolic blood pressure.<sup>10</sup> This was then repeated during the first 24 hours after the procedure. The number of patients experiencing episodes of hypotension or hypertension after CEA or endovascular treatment was documented, and the difference between the 2 procedures was assessed. An episode of hypotension was defined as a fall in systolic blood pressure of  $>30$  mm Hg, and an episode of hypertension was defined as a rise in systolic blood pressure of  $>30$  mm Hg from the baseline blood pressure reading. If the fall in systolic blood pressure was sustained for  $>1$  hour, it was then defined as persistent hypotension. Twenty-four-hour blood pressure recordings were also taken at 1 and 6 months.

### Statistical Analysis

Baseline systolic blood pressure was derived from the average reading of the preprocedure 24-hour ambulatory blood pressure recordings. The 2 groups were compared with an independent *t* test. The number of patients who experienced episodes of hypotension or hypertension was recorded, and the time that the first episode of hemodynamic disturbance occurred was noted. The difference between the 2 groups was compared with the  $\chi^2$  or Fisher exact test.

The average systolic and diastolic blood pressure at each hourly interval for both groups was calculated for the first 24 hours. Comparisons with preprocedure values were made with the paired *t* test. An ANCOVA with a general linear model, with group and time point as fixed factors, was used to compare both groups in the first 24 hours after the procedures.

**TABLE 1. Baseline Characteristics**

	Surgery (n=49)	Endovascular (n=54)
Age (mean)	66	68
Male sex (%)	63.3	66.7
Hypertension (%)	44.9	50.0
Peripheral vascular disease (%)	24.5	25.9
Diabetes (%)	10.2	11.1
Smoker current/ex (%)	83.7	81.5
Ischemic heart disease (%)	38.8	46.3
Atrial fibrillation (%)	6.1	5.6
Presenting symptoms (%)		
Amaurosis fugax	38.8	37.0
Retinal occlusion	6.1	1.9
TIA	26.5	27.8
Minor stroke	2.0	11.1
Nondisabling stroke	12.2	13.0
Disabling stroke	12.2	9.3
None (pre-CABG)	2.0	0

TIA indicates transient ischemic attack; CABG, coronary artery bypass grafting.

The average systolic and diastolic blood pressure was also calculated for 1 and 6 months for both groups. Comparisons with preprocedure values were made with the paired *t* test.

We also performed a subgroup analysis of the endovascular group, taking into account the change of technique from PTA alone to angioplasty with carotid artery stenting and from balloon-expandable stents to self-expanding stents.

The threshold for statistical significance was taken as  $P<0.05$ .

## Results

Table 1 summarizes the clinical characteristics of the 103 patients who participated in this study (surgery, n=49; endovascular treatment, n=54). The total number of procedures performed was 104, since 1 patient was treated twice with carotid angioplasty. One value for the preprocedure (endovascular) 24-hour blood pressure data was not available because of technical failure and was excluded from further analysis. The baseline average blood pressure for both groups was not significantly different (systolic blood pressure; 95% CI,  $-1.63$  to  $10.82$ ;  $P=0.15$ ).

In the immediate postprocedural period, 5 patients (all surgical) were excluded from analysis because postprocedural 24-hour blood pressure data were not available as a result of technical failure of the blood pressure monitoring equipment.

Episodes of hypotension were seen frequently in both groups (75.0% in the surgical group and 75.9% in the endovascular group;  $P=0.92$ ). The number of patients in each group who experienced a hypertensive episode was also similar: 11.4% in the surgical group versus 13.0% in the endovascular group ( $P=0.81$ ). No patients in the endovascular group received the phenylephrine/esmolol regimen, whereas 33 patients in the surgical group received phenylephrine and 5 patients received esmolol. Persistent hypotension occurred in 50.0% of the surgical group and 44.4% of the endovascular group ( $P=0.58$ ).

TABLE 2. Average Blood Pressures (mm Hg)

	First 24 Hours				1 Month		6 Months	
	Pre	Pre	1 Hour	20 Hours	Pre	1 Month	Pre	6 Months
<b>Surgery</b>								
No.	49	37	...	...	35	...	31	...
Systolic	146.0	145.9	121.6*	146.1	145.9	140.1†	145.8	140.9†
Diastolic	80.2	80.4	69.5*	79.8	80.4	78.0	80.4	77.7
<b>Endo</b>								
No.	54	48	...	...	48	...	39	...
Systolic	141.4	142.2	126.0*	118.4*	140.9	138.2	139.8	137.9
Diastolic	78.4	78.9	73.4*	63.4*	78.3	77.4	78.5	77.7
<b>PTA</b>								
No.	30	28	...	...	...	26	...	18
Systolic	143.4	144.0	126.2	123.6	...	139.6	...	140.9
Diastolic	79.4	79.9	73.6	65.2	...	77.0	...	80.2
<b>CAS</b>								
No.	24	20	...	...	...	22	...	21
Systolic	138.9	139.6	125.8	112.8	...	136.7	...	135.3
Diastolic	77.0	77.6	73.2	61.4	...	77.4	...	75.6
<b>Self</b>								
No.	11	11	...	...	...	10	...	10
Systolic	136.0	136.0	131.3	114.3	...	135.6	...	136.3
Diastolic	77.6	77.6	74.8	66.9	...	77.6	...	76.9

Numbers in the "Pre" columns represent the total No. analyzed. Paired *t* tests were performed on the surgical and endovascular groups only. Endo indicates endovascular; CAS, carotid artery stenting; and Self, self-expanding stent.

\*The change in blood pressure was statistically significant ( $P<0.001$ ).

†The change in blood pressure was statistically significant ( $P<0.05$ ).

### Immediate Changes

Accurate timing of hemodynamic disturbance after carotid intervention did not occur in 13 procedures (7 surgical, 6 endovascular), and therefore these were not included in this analysis. The first significant hemodynamic change in blood pressure occurred at or before 6 hours in 89.7% of the surgical group and in 73.2% of the endovascular group ( $P=0.09$ ). This occurred at or before 10 hours in 93.1% of the surgical group and in 85.4% of the endovascular group ( $P=0.46$ ).

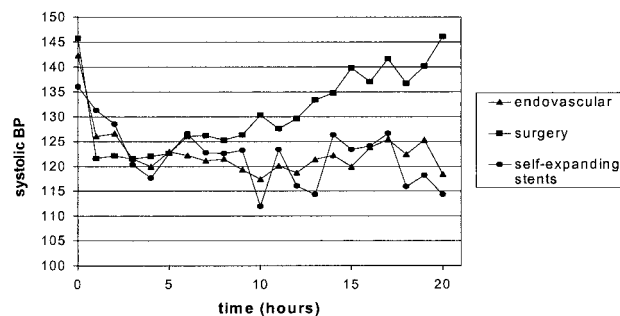
At 1 hour there was a significant fall in blood pressure for both groups from baseline (surgical group mean systolic difference, 24.3 mm Hg; 95% CI, 17.1 to 31.5;  $P<0.001$ ; endovascular group mean systolic difference, 16.2 mm Hg; 95% CI, 9.5 to 22.9;  $P<0.001$ ) (Table 2).

Because of a marked reduction in data obtained at 24 hours (<50%), the average fall in blood pressure was compared at 20 hours. The surgical group's blood pressure returned to baseline, but there was a sustained fall in blood pressure in the endovascular group (surgical group mean systolic difference,  $-0.8$  mm Hg; 95% CI,  $-12.7$  to 11.1;  $P=0.89$ ; endovascular group mean systolic difference,  $-22.6$  mm Hg; 95% CI,  $-15.3$  to  $-30.1$ ;  $P<0.001$ ).

Overall, when the 2 groups were assessed over the 24-hour time period, the difference in blood pressure response was highly significant (95% CI, 15.2 to 33.8;  $P<0.0001$ , ANCOVA) (Figure).

### Changes at 1 Month

At 1 month, data were available for 92 procedures (41 in surgery group, 51 in endovascular group). Medication changes occurred in 8 patients (6 in surgery group, 2 in endovascular group), and these were omitted from analysis in addition to the patient who had no preprocedure 24-hour recording for comparison. In the surgical group there was a significant reduction in blood pressure (95% CI, 0.9 to 10.8;  $P<0.05$ ). There was no difference in systolic blood pressure from preprocedure values in the endovascular group (95% CI,  $-0.91$  to 6.5;  $P=0.14$ ) (Table 2).



Mean hourly systolic blood pressure after CEA ( $n=37$ ), endovascular treatment ( $n=48$ ), and self-expanding stents ( $n=11$ ). The difference between the surgical and endovascular groups is highly significant ( $P<0.0001$ , ANOVA).

**TABLE 3. Neurological Complications**

Procedure	Event	Hemodynamic disturbance
PTA	CRAO	None
PTA	Branch CRAO	Hypotension
PTA	Branch CRAO	Sustained hypotension
PTA	TIA	Hypotension
PTA	TIA	Sustained hypotension
PTA	TIA	Hypertension
CAS (self-expandable stent)	TIA	Hypotension
CAS (balloon-expandable stent)	Minor stroke	Sustained hypotension
CAS (self-expandable stent)	Intracranial hemorrhage and death	Sustained hypotension
CAS (balloon-expandable stent)	Intracranial hemorrhage and death	Sustained hypotension
CEA	Major nondisabling stroke	Sustained hypotension
CEA	Major nondisabling stroke	Sustained hypotension
CEA	Major nondisabling stroke	Sustained hypotension
CEA	Major nondisabling stroke	Sustained hypotension

There was an additional death within 30 days of CEA secondary to malignancy; it was not associated with hemodynamic change. CAS indicates carotid artery stenting; CRAO, central retinal artery occlusion; and TIA, transient ischemic attack.

### Changes at 6 Months

At 6 months, data were available for 77 procedures (37 in surgery group, 40 in endovascular group); a total of 7 patients were excluded from analysis because of changes in medication (6 in surgery group, 1 in endovascular group). There was a significant reduction in blood pressure in the surgical group (95% CI, 0.31 to 9.5;  $P<0.05$ ); however, there was no difference in systolic blood pressure in the endovascular group (95% CI,  $-0.8$  to 2.6;  $P=0.29$ ) (Table 2).

### Endovascular Group

PTA alone was performed on 31 patients (1 was excluded from analysis because of lack of preprocedure data; see above). Twenty-four patients underwent carotid artery stenting; of these, 7 were secondary and 17 were primary stenting procedures. The use of balloon-expandable stents occurred in 13 patients, and self-expanding stents were used in 11 patients.

There was no difference in frequency of hypotensive events between PTA and carotid artery stenting groups (76.7% and 75.0%, respectively;  $P=1$ ). Persistent hypotension occurred in 43.4% of the PTA group and 45.8% of the carotid artery stenting group ( $P=1$ ). The baseline average blood pressures for both groups were not significantly different. However, when the 2 groups were assessed over the 24-hour time period, the difference in blood pressure response was highly significant (95% CI, 30.1 to 51.2;  $P<0.0001$ , ANCOVA), with a lower blood pressure sustained over the first 24 hours in the carotid artery stenting group. No long-term blood pressure differences were seen between the PTA and carotid artery stenting groups (Table 2).

There was no difference in frequency of hypotensive events between balloon-expandable and self-expandable stent groups (72.7% and 76.9%, respectively;  $P=1$ ). However, persistent hypotension occurred in 61.5% of the balloon-expandable stent group and 27.3% of the self-expandable stent group ( $P=0.12$ ). The baseline average blood pressures for both stent types were

not significantly different. However, when the 2 stent types were assessed over the 24-hour time period, the difference in blood pressure response was highly significant (95% CI, 37.9 to 57.0;  $P<0.0001$ , ANCOVA), with the balloon-expandable stent resulting in lower systolic blood pressures.

### Neurological Complications

Within the perioperative period (ie, first 30 days), the all stroke/death rates were 10.2% in the surgical group and 5.5% in the endovascular group.

Of those who experienced a hemodynamic disturbance, 16.0% had a neurological complication in the perioperative period, including all transient ischemic attack, amaurosis fugax, stroke, and stroke-related death. Only 5.9% of those who were hemodynamically stable did so. This was not statistically significant ( $P=0.46$ , Fisher exact test) (Table 3).

### Excluded Data

The baseline characteristics of the patients excluded in the immediate analysis did not vary from the baseline characteristics of those retained. The 30-day outcome for this group included 2 nondisabling major strokes only. Therefore, the neurological complication rate and the all stroke/death rate were both 10.5%. For the remaining procedures, the 30-day neurological complication rate and the all stroke/death rate were 14.1% and 7.1%, respectively.

The reasons for loss of data at 1 and 6 months included death ( $n=4$ ), stroke ( $n=1$ ), move from the country ( $n=1$ ), inaccurate timing of data ( $n=5$ ), refusals ( $n=19$ ), and surgical procedure ( $n=1$ ).

### Discussion

This is a hypothesis-generating study that demonstrates that hemodynamic disturbances in the acute postprocedural period are frequently experienced after both surgical and endovascular treatment of carotid stenosis. Although statistical comparisons

have been presented, they should be reviewed in the context of the limitations of the study. The occurrence of episodes of hypotension or hypertension does not appear to differ between the 2 groups, but the overall pattern of change in blood pressure was seen to be different. In the surgical group there was a reduction in blood pressure at 1 hour, but this then recovered quickly. However, by 1 month there was a fall in systolic blood pressure that was sustained at 6 months. This differed from the changes seen in the endovascular group, in which there was a sustained fall in blood pressure in the immediate postprocedural period that recovered to preprocedure levels by 1 month and was unchanged at 6 months.

This study has several important strengths. It is the first to compare the effects on blood pressure of both CEA and endovascular treatment of carotid artery stenosis, and the blood pressure measurements were obtained prospectively. To help eliminate factors that reduce the reliability of single blood pressure values, such as "white coat effect," time of measurement, and interrater reliability, 24-hour blood pressure readings were used both before and after the procedure.<sup>11</sup>

Although the baseline systolic blood pressure is slightly lower in the endovascular group, it is the change in blood pressure from each group's baseline that is highly significant. Interpretation of results must take into account, however, that the postoperative care differed between the 2 groups. The surgical patients were monitored on a high-dependency unit and consequently had more active management of blood pressure. This would not have altered the initial documentation of an occurrence of hemodynamic disturbance because pharmacological intervention was only triggered if the change in systolic blood pressure was  $>30$  mm Hg. Nevertheless, the treatment received by the surgical group could potentially result in further hemodynamic disturbance or limit the degree of disturbance; this may explain the difference seen between the 2 groups. However, despite this intervention, persistent hypotension was still observed in 50% of the surgical group. Furthermore, the surgical procedure was standardized throughout the study period, but the endovascular technique varied, with 44% of patients having stent insertion. Separate analysis of these patients was therefore performed. Medication changes that potentially had effects on blood pressure occurred in 9 patients in the 6-month follow-up period. In 4 patients changes were made for reasons not related to blood pressure management, in 1 patient antihypertensive drugs were stopped because of prolonged hypotension, and 4 patients were treated for hypertension. Since these changes were a potential source of bias, these patients were omitted from analysis. However, the inclusion of these patients does not change the results except that the reduction in 6-month diastolic blood pressure in the surgical group would reach statistical significance (mean diastolic difference, 3.4 mm Hg; 95% CI, 0.7 to 6.1;  $P<0.05$ ). A limitation of this study is the reduction in data seen within the first 24 hours but particularly at 1 and 6 months. This is unfortunate in that this represents a potential source of bias and limits any definite conclusion being drawn.

Hemodynamic disturbances immediately after carotid intervention are well recognized. Hypertension has been noted with a frequency of 9% to 38% after CEA<sup>2,12</sup> and 39% after carotid stent insertion.<sup>7</sup> A wide variation in the frequency of hypotension has been observed (12% to 50% after endarterectomy<sup>1,2</sup> and

18.8% to 56.1% after endovascular intervention<sup>6,8</sup>). In this study a low frequency of episodes of hypertension was noted (11.4% after surgery, 13.0% after endovascular treatment), but a much higher frequency of episodes of hypotension was observed (75.0% after surgery and 75.9% after endovascular treatment). The wide variation in frequency of blood pressure fluctuations seen in other studies and the high incidence of hypotensive episodes observed in this study may be explained in part by the definitions used. A strict definition of a change of  $>30$  or  $<30$  mm Hg was chosen for our study because this was the degree of change previously allowed in postsurgical patients before active treatment was given. Persistent hypotension lasting  $>1$  hour was also assessed because this has previously been shown to relate to adverse neurological outcome,<sup>6</sup> although the magnitude of the change in systolic blood pressure ( $>50$  mm Hg) has recently also been shown to relate to adverse neurological events after carotid stenting.<sup>13</sup> Comparison between the 2 groups in this regard was subject to bias because the surgical group received more active treatment. Furthermore, the surgical technique can influence the type of blood pressure disturbances seen, so that dissection methods that preserve the carotid nerve result in fewer episodes of hypertension.<sup>1</sup> The methods used in this study would favor hypotensive rather than hypertensive changes.

The initial difference in blood pressure response between the 2 groups is interesting. During CEA, removal of the atheromatous plaque reduces pressure wave dampening, thus increasing baroreceptor stimulation, resulting in hypotension.<sup>14</sup> The more sustained fall seen in the endovascular group may be explained partly by increased distension of the carotid sinus from compression of the atherosclerotic plaque during balloon angioplasty. Further stimulation may also result from additional pressure exerted by a stent. In this study both angioplasty alone and carotid artery stenting result in a sustained reduction in systolic blood pressure in the immediate postprocedural period, which was more pronounced when a stent was used. Persistent hypotension has been found to be more frequent after the use of balloon-expandable rather than self-expanding stents.<sup>6</sup> This is due to the fact that balloon-expandable stents are less flexible and have a stronger radial force. Although the number of episodes of hypotension did not differ between the 2 types of stent in this study, a greater proportion of patients in the balloon-expandable group experienced persistent hypotension. There was a highly significant difference seen in blood pressure response in the balloon-expandable group, with a more marked lowering of systolic blood pressure over the first 24 hours. Current endovascular practice is based on the use of self-expandable stents; the effect on blood pressure with the use of these stents in the immediate perioperative period is shown in the Figure.

Although the increase in baroreceptor activity is thought to be a short-term phenomenon, the baroreceptors can be reset to function at higher levels secondary to age, atherosclerosis, or chronic hypertension.<sup>15</sup> The change in vessel wall and removal of the atherosclerotic plaque after surgery may cause further resetting of the baroreceptors and hence a long-term fall in blood pressure. Previous studies assessing blood pressure changes at 6 months and 2 years after endarterectomy did not find a long-term effect; however, 24-hour blood pressure monitoring was not

used.<sup>16,17</sup> A study that used 24-hour ambulatory monitoring also found a reduction in blood pressure 2 weeks after endarterectomy.<sup>18</sup>

Blood pressure management plays a crucial role in the prevention of stroke. Any decrease in blood pressure is associated with a decrease in the relative risk of stroke.<sup>19</sup> A study of antihypertensive treatments in patients with a previous history of cerebrovascular events found that a reduction of 9/4 mm Hg was associated with a reduced risk of stroke of 28%, and therefore even small decreases in blood pressure are highly effective.<sup>20</sup> Blood pressure instability in the immediate postprocedural period is a common occurrence after both CEA and the endovascular treatment of carotid artery stenosis. The long-term effect, however, requires further confirmation to assess whether endarterectomy rather than endovascular treatment is associated with a sustained reduction. Despite this, regular monitoring of blood pressure should continue to play a key role in ongoing management for both groups since the importance of blood pressure control for all patients at risk of cerebrovascular disease cannot be overemphasized.

## References

- Cafferata HT, Merchant RF, DePalma RG. Avoidance of post carotid endarterectomy hypertension. *Ann Surg.* 1982;196:465–472.
- Wong JH, Findlay JM, Suarez-Almazor ME. Hemodynamic instability after carotid endarterectomy: risk factors and associations with operative complications. *Neurosurgery.* 1997;41:35–43.
- Towne JB, Bernhard VM. The relationship of postoperative hypertension to complications following carotid endarterectomy. *Surgery.* 1980;88:575–580.
- CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. *Lancet.* 2001;357:1729–1737.
- Brooks WH, McClure RR, Jones MR, Coleman TC, Breathitt L. Carotid angioplasty and stenting versus carotid endarterectomy: randomized trial in a community hospital. *J Am Coll Cardiol.* 2001;38:1589–1595.
- Dangas G, Laird JR, Satler LF, Mehran R, Mintz GS, Larrain G, Lansky AJ, Gruberg L, Parsons EM, Laureno R, et al. Postprocedural hypotension after carotid artery stent placement: predictors and short- and long-term clinical outcomes. *Radiology.* 2000;215:677–683.
- Qureshi AI, Luft AR, Sharma M, Janardhan V, Lopes DK, Khan J, Guterman LR, Hopkins LN. Frequency and determinants of postprocedural hemodynamic instability after carotid angioplasty and stenting. *Stroke.* 1999;30:2086–2093.
- Gil-Peralta A, Mayol A, Gonzalez Marcos JR, Gonzalez A, Ruano J, Boza F, Duran F. Percutaneous transluminal angioplasty of the symptomatic atherosclerotic carotid arteries: results, complications, and follow-up. *Stroke.* 1996;27:2271–2273.
- Beard JD, Mountney J, Wilkinson JM, Payne A, Dicks J, Mitton D. Prevention of postoperative wound haematomas and hyperperfusion following carotid endarterectomy. *Eur J Vasc Endovasc Surg.* 2001;21:490–493.
- O'Brien E, Atkins N, Staessen J. State of the market: a review of ambulatory blood pressure monitoring devices. *Hypertension.* 1995;26:835–842.
- Zanchetti A. The role of ambulatory blood pressure monitoring in clinical practice. *Am J Hypertens.* 1997;10(pt 1):1069–1080.
- Wade JG, Larson CP, Hickey RF, Ehrenfield WK, Severinghaus JW. Effect of carotid endarterectomy on carotid chemoreceptor and baroreceptor function in man. *N Engl J Med.* 1970;282:823–829.
- Howell M, Krajcer Z, Dougherty K, Strickman N, Skolkin M, Toombs B, Paniagua D. Correlation of periprocedural systolic blood pressure changes with neurological events in high-risk carotid stent patients. *J Endovasc Ther.* 2002;9:810–816.
- Angell-James JE, Lumley JSP. The effects of carotid endarterectomy on the mechanical properties of the carotid sinus and carotid sinus nerve activity in atherosclerotic patients. *Br J Surg.* 1974;61:805–810.
- Chapleau MW, Cunningham JT, Sullivan MJ, Wachtel RE, Abboud FM. Structural versus functional modulation of the arterial baroreflex. *Hypertension.* 1995;26:341–347.
- Dehn TCB, Angell-James JE. Long-term effect of carotid endarterectomy on carotid sinus baroreceptor function and blood pressure control. *Br J Surg.* 1987;74:997–1000.
- Eliasziw M, Spence JD, Barnett HJ. Carotid endarterectomy does not affect long-term blood pressure observations from the NASCET: North American Symptomatic Carotid Endarterectomy Trial. *Cerebrovasc Dis.* 1998;8:20–24.
- Dodds SR, Finch D, Chant ADB. Early effect of carotid endarterectomy on arterial blood pressure measured with an ambulatory monitor. *Br J Surg.* 1997;84:1104–1106.
- MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, Abbott R, Godwin J, Dyer A, Stamler J. Blood pressure and coronary heart disease, part 1: prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet.* 1990;335:765–774.
- PROGRESS Collaborative Group. Randomised trial of a perindopril based blood pressure lowering regimen among 6105 individuals with a previous stroke or transient ischaemic attack. *Lancet.* 2001;358:1033–1041.

## Editorial Comment

### Hypotension After Carotid Revascularization

Carotid artery stenosis typically involves accumulation of hard calcified atheroma at the common carotid artery bifurcation with involvement of the origin of the internal carotid artery. Anatomically, this location is in close proximity to the area where the carotid baroreceptors are located. The function of these receptors is to sense the tension exerted on the arterial wall and provide feedback control to blood pressure regulation centers.

In patients with carotid artery stenosis requiring revascularization, the mere presence of calcified atheroma in this specific arterial location has chronically “sensitized” the carotid baroreceptors to very small changes in carotid artery tension. (The thicker and more calcified the wall, the more rapid and efficient pressure/energy transmission it allows.) Therefore, external manipulation of this area during surgery,

as well as the transmission of the luminal distention through the arterial wall during balloon inflation and stent expansion, can produce a hypotensive response. This phenomenon varies with (1) the intensity of manipulation or distention of the artery and (2) plaque burden and plaque composition (thickness and calcification).

Development of significant hypotension has been linked with neurological complications after carotid stent procedures.<sup>1,2</sup> “Persistent profound hypotension” was defined as a >40 mm Hg decrease in arterial pressure without evidence of hypovolemia, with a systolic pressure <90 mm Hg at the end of the procedure and lasting at least 1 hour<sup>1</sup>; in the other study, “severe hypotension” was defined as a pressure drop of at least 50 mm Hg.<sup>2</sup> Lower levels of hypotension were inconsequential in relation to the patient’s neurological status.

This phenomenon was “explained” by the use of aggressive balloon dilatation and the use of balloon-expandable stents.<sup>1</sup>

### Findings

In this issue of *Stroke*, McKeivitt et al attempted to address this subject in a patient population who was enrolled in the randomized trial CAVATAS of carotid angioplasty versus surgical endarterectomy.<sup>3,4</sup> This is the first specific report of the effects of surgery on arterial blood pressure during and after carotid revascularization. Continuous (24-hour) blood pressure monitoring was employed in the subset of patients who consented to this substudy in a single center. Furthermore, long-term follow-up was available. All these advantages really provided the foundation of a very essential experimental protocol.

The findings of this study<sup>3</sup> mainly confirmed previous observations<sup>1,2</sup>: (1) “any” pressure drop >30 mm Hg occurred in similar degrees among the various types of endovascular procedures and was very frequent (>75%); (2) aggressive angioplasty and balloon-expandable stent deployment produced persistent hypotension more frequently than the currently accepted approach of gentle dilation with self-expanding stent deployment (62% versus 27%); (3) hypotension had a trend to correlate to neurological complications (16% versus 6% for patients without hypotension).

With respect to endovascular approach versus surgery in this study,<sup>3</sup> the endovascular approach had (1) fewer neurological complications overall (5.5% versus 10.2%), (2) more hypotension episodes defined as a blood pressure drop of at least 30 mm Hg, and (3) higher blood pressure at follow-up (mean difference of 5 mm Hg).

The above-quoted percentage comparisons were found to be not statistically significant due to very small sample size, but they are arithmetically so far apart from each other and they qualitatively concurred with recent investigation on these subjects.<sup>1,2</sup> (Results of the SAPHIRE Randomized Trial were presented by J. Yadav, MD, at the AHA 2002 Annual Scientific Sessions, Chicago, Ill, November 2002.)

### Shortcomings

The acute hemodynamic differences in the 2 groups are difficult to explain because a very specific protocol to aggressively treat hypotension in the surgical group was employed (with use of intravenous pressors in one third of surgical patients), whereas no such protocol existed for the angioplasty group. This biased methodology is rather surprising given that this study was specifically designed to evaluate blood pressure fluctuation during and after the procedure in both treatment arms. It seems as though 1 arm (surgery) was specifically “assisted” in avoiding and aggressively treating hypotension.

The follow-up blood pressure results are also difficult to interpret but are a very useful foundation for further investigation. The intensity of long-term antihypertensive therapy was not specifically assessed (number and dosage of medications). Thus, it is unclear whether the observed differences in blood pressure control were due to the carotid procedure or to confounders related to the outpatient management of blood pressure.

Third, the major limitation of the main randomized trial<sup>4</sup> as well as the present substudy<sup>3</sup> is the fact that the endovascular

approach has already evolved to improved techniques that are underrepresented in the present investigational report (due to the time lapse between trial planning and presentation of results): aggressive angioplasty with provisional stenting and deployment of balloon-expandable stents with high-pressure postdilatation (the CAVATAS protocol) are no longer used, and it is really surprising that such “abandoned” techniques in fact managed to achieve equal neurological complication rates to surgery in the main study<sup>3</sup> and almost half in the present substudy!<sup>4</sup>

### Hypotension: Does It Matter?

With respect to hypotension, I would summarize the “take-home” messages as follows: (1) severe or persistent hypotension correlates to adverse neurological events; (2) mild hypotension is very frequent during carotid procedures, and therefore rather nonspecific as a marker of complications; (3) aggressive treatment of hypotension during surgery did not seem to result in low neurological complications in the present study.

Still, it is unclear if preventing hypotension will prevent neurological events after carotid revascularization. It is difficult to believe that hypotension itself causes a focal neurological event, but it would be easier to adopt that profound hypotension may render a potentially inconsequential (under normal hemodynamics) microembolization into a clinically detectable neurological event. In addition, hypotension can be specifically detrimental in patients with severe coronary stenosis. Finally, hypotensive response after carotid procedure may represent a confounder that characterizes high-risk patients with generalized atherosclerosis and marked arterial stiffness. Given all these possibilities, it is recommended that hypotension should be treated aggressively during carotid procedures so that it is aborted when “mild” before it becomes “severe” or “persistent” as defined above.<sup>5</sup> Clearly, further investigation is required with respect to the long-term implication of blood pressure fluctuations during or shortly after carotid procedures.

**George Dangas, MD, PhD, Guest Editor**

*Cardiovascular Research Foundation  
Lenox Hill Heart & Vascular Institute of New York  
New York, NY*

### References

1. Dangas G, Laird JR Jr, Satler LF, et al. Postprocedural hypotension after carotid artery stent placement: predictors and short- and long-term clinical outcomes. *Radiology*. 2000;215:677–683.
2. Howell M, Krajcer Z, Dougherty K, et al. Correlation of periprocedural systolic blood pressure changes with neurological events in high-risk carotid stent patients. *J Endovasc Ther*. 2002;9:810–816.
3. McKeivitt FM, Sivaguru A, Venables GS, et al. How the treatment of carotid artery stenosis affects blood pressure: a comparison of hemodynamic disturbances following carotid endarterectomy and endovascular treatment. *Stroke*. 2003;34:2576–2582.
4. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. *Lancet*. 2001;357:1729–1737.
5. Roubin GS, New G, Iyer SS, et al. Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis: a 5-year prospective analysis. *Circulation*. 2001;103:532–537.