ORIGINAL RESEARCH

M.B. Sánchez-Arjona
G. Sanz-Fernández
E. Franco-Macías
A. Gil-Peralta

Cerebral Hemodynamic Changes after Carotid Angioplasty and Stenting

BACKGROUND AND PURPOSE: Carotid angioplasty stent placement (CAS) is an accepted alternative to endarterectomy. However, little is known about its effect on cerebral hemodynamics. We prospectively studied the early and delayed hemodynamic changes after CAS.

MATERIALS AND METHODS: Sixty patients underwent CAS for ≥70% internal carotid artery stenosis. Transcranial Doppler (TCD) was done before, 6 hours, and 30 days after CAS. Cerebrovascular reserve to apnea (CVR) was measured.

RESULTS: On the ipsilateral side, basal middle cerebral artery (MCA) middle flow velocity (MFV) and pulsatility index (PI) increased from 49.7 cm/s and 0.85, respectively, to 62.5 cm/s and 1.09 immediately after CAS ($P < .05$); anterior cerebral artery (ACA) MFV and PI increased from 50.7 cm/s and 0.90, to 58.9 cm/s and 1.08 ($P < .05$); and posterior cerebral artery (PCA) MFV decreased from 47.5 to 36.5 cm/s, with no change in PI ($P < .05$). On the contralateral side, nonsignificant changes were seen on MCA, immediately after CAS; ACA and PCA MFV decreased from 63.7 and 45.3 cm/s to 50.3 and 38.6 cm/s, respectively ($P < .05$); ACA and PCA PI increased from 0.96 and 1.00, respectively, to 1.04 and 1.04 ($P < .05$). At 30 days, ipsilateral MCA MFV and PI were 52.8 cm/s and 1.12, respectively ($P < .05$), and contralateral values were 49.6 cm/s ($P < .05$) and 1.02 (nonsignificant), respectively. Basal ipsilateral and contralateral CVR improved from 26.0% to 37.0% ($P < .05$), and from 30.1% to 33.5% (nonsignificant), respectively, at 30 days.

CONCLUSIONS: CAS produces an early significant increase of MFV and PI in the ipsilateral anterior circulation. This effect is maintained, though minor, 30 days later. In addition, CAS results in an improvement of CVR at 30 days.

During the last 2 decades, percutaneous transluminal angioplasty and stent placement have become a therapeutic alternative to carotid endarterectomy (CEA) in the treatment of carotid stenosis.[1,2] Although both the risk and benefit of carotid angioplasty stent placement (CAS) have been studied,[3,4] little is known about hemodynamic changes that occur immediately after CAS. Most reports describe hemodynamic changes after CEA[5-9] with interest being focused on the side of the operation and on perioperative and postoperative complications, such as hyperperfusion syndrome (HS) and intracerebral hemorrhage.[10-13] The hemodynamic changes in the middle cerebral artery (MCA) flow velocity early after CAS have been less studied, and the number of patients in these reports was low.[14-17] Those changes might be different, both in time and significance, from those produced by CEA, as several variables, such as the carotid occlusion time or the use of anesthesia, are lesser or avoided in CAS. Cerebral hemodynamics can be evaluated by transcranial Doppler (TCD). This simple noninvasive technique provides information on blood flow velocities in larger cerebral vessels and also has proved to be reliable to evaluate the cerebrovascular reserve (CVR).[18,19]

The purpose of this study was to assess, in the entire circle of Willis, the immediate and delayed effects of CAS on cerebral hemodynamics, with the use of TCD. With this data and the knowledge of basal CVR, basal middle flow velocity (MFV), and pulsatility index (PI) of the main cerebral arteries, we could identify hemodynamic patterns of patients who are at higher risk or those who benefit most from carotid interventional therapy.

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From the Neurology and Neurophysiology Department (M.B.S.-A., E.F-M., A.G.-P.), University Hospital Virgen del Rocío, Seville, Spain; and Neurology Department (G.S.-F.), Hospital Juan Ramón Jiménez, Huelva, Spain.

Address correspondence to María Bernal Sánchez-Arjona, Neurology and Neurophysiology Department, 1st floor HRT, University Hospital Virgen del Rocío, Av Manuel Siurot sn, 41013 Seville, Spain; e-mail: mbs-a@ole.com

Patients and Techniques

Ninety patients with atheromatous stenosis ≥70% according to North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria[1] underwent CAS from January 2003 to March 2004. Mean age was 66 ± 9 years, and 52 subjects were male. Table 1 shows the demographic data. All patients were consecutively selected for CAS because, during that period, no vascular surgeons with enough expertise were available in our hospital. Sixty of the 90 were included. Of them 54 (90%) were symptomatic. Six asymptomatic patients were included because of reduced CVR and insufficient collateral flow. Eighteen (20.0%) patients were excluded because of absence of bone window, 9 (10.0%) for intracranial tandem carotid stenosis, and 3 (3.3%) because follow-up was considered impossible. The hospital ethics committee approved the project, and all patients gave their informed consent.

Carotid stenosis was assessed by duplex sonography and confirmed by arteriography. Cerebral CT or MR imaging was done in all patients. We noted demographic data including age, sex, vascular risk factors, concomitant vascular disease, type of ischemia previous to CAS, and time between the ischemic event and the procedure. TCD and breath-holding test (BHT)[19-21] were performed the day before CAS. Treatment with aspirin 125 mg/day and clopidogrel 75 mg/day was begun at least 72 hours before CAS. Patients also received a full dose of IV heparin.

Four-vessel angiography was done immediately before CAS to confirm the degree of stenosis, to evaluate the efficacy of the ipsilateral flow, and to assess the collateral supply. This supply was considered adequate when both communicant arteries, or even the ophthalmic artery or the leptomeningeal anastomosis and 1 communicant artery,

Table 1: Patient demographic data, type of ischemia previous CAS and collateral pathways

Finding	No. of Patients (%)
Sex	
Male	52 (80.0)
Female	8 (10.0)
Vascular risk factors and vascular disease	
Hypertension	47 (78.3)
Diabetes mellitus	28 (46.7)
Hyperlipemia	41 (68.3)
Smoke	26 (43.3)
Ischemic cardiopathy	16 (26.7)
Peripheral arterial disease	17 (28.3)
Type of ischemia before CAS	
Transient ischemic attack (including amaurosis fugax)	33 (55.0)
Minor stroke	15 (25,0)
Major stroke (ranking ≥2)	11 (18.3)
Asymptomatic	6 (10.0)
Concomitant vasculopathy	
Contralateral ICA stenosis	35 (58.3)
Contralateral ICA occlusion	10 (16.7)
Vertebral artery stenosis	10 (16.7)
Collateral pathways	
Ophthalmic	14 (23.3)
Anterior crossflow	48 (80.0)
Posterior	33 (55.9)
Leptomeningeal	4 (6.7)

Note:—CAS indicates carotid angioplasty stent placement; ICA, internal carotid artery.

were patent and cooperate to get an efficient flow in the ipsilateral arteries. The procedure was carried out according to our protocol[22,23] with stent placement and distal protection in all cases. After CAS, patients were monitored in the Stroke Unit for 24 hours. IV heparin was started 3 hours after CAS and maintained for 24 hours. We recorded arterial pressure, heart rate, neurologic symptoms, and femoral puncture site complications. Neurologic complications during and after the procedure were classified as transient ischemic attacks (TIA), minor stroke or stroke lasting less than 7 days, and major stroke. We also registered symptoms of hyperperfusion, such as headache, seizures, confusion, neurologic deficit, and high blood pressure (systolic blood pressure >150 mm Hg and/or diastolic blood pressure >90 mm Hg).[12,24,25] We considered the occurrence of headache or hypertension during or after CAS as oligosymptomatic cases of HS, whereas a complete HS would show the rest of symptoms already mentioned. TCD was performed within 6 hours after stent placement. An increase in MFV of more than 100% after stent placement predicts HS.[12]

The next day, a duplex sonography of the stented vessel was performed. Patients were discharged on aspirin 125 mg/day or triflusal 600 mg/day and clopidogrel 75 mg/day for a month. Aspirin or triflusal was continued indefinitely. On day 30, TCD and BHT were repeated.

Transcranial Doppler

Blood flow velocities were measured using a 2-MHz TCD. All examinations were done by the same person to maintain a constant angle of insonation. MCA and anterior cerebral arteries (ACA) were insonated through the temporal window at depths of 50–60 mm and 65–75 mm, respectively. Posterior cerebral arteries (PCA) were insonated at a depth of 60–75 mm. Ipsilateral and/or contralateral carotid compression was performed when needed to accurately identify the insonated vessel. MFVs time-averaged peak frequencies of the envelope curve of the Doppler spectrum) and PI (systolic velocity minus diastolic velocity divided by MFV) were recorded the day before CAS, within 6 hours after the procedure, and 30 days later. Blood pressure was measured at each examination using a regular cuff.

TCD measurement of CVR was performed using the BHT. This test uses the increase of arterial P_{CO_2} induced by breath holding, as a vasodilative stimulus. This is a simple procedure because it is not necessary, neither the inhalation of 5% CO_2 nor the measurement of end-expiratory CO_2.[20,26] We performed the technique as breath holding for a minimum of 15 seconds after normal inspiration, and we repeated it twice to assure the patient was doing it right. We obtained TCD measurements with bilateral fixed probes and used the percentage increase of MFV in the MCA without consideration of the time of breath holding.[20,21] We chose this measurement because it correlates the best with the MFV increase in the acetazolamide test, and in our experience, time calculations are unnecessary.[21] A percentage increase of MFV inferior to 20% was considered impaired CVR.[27]

Statistical Analysis

We used SPSS version 11.5 software (SPSS, Chicago, Ill) for analysis. Results were expressed as means ± SD and percentages. We confirmed the normal distribution of our data by Kolgomorov-Smirnov test. Changes in hemodynamics, MFV, PI, and CVR before and after CAS were evaluated with the use of a paired *t* test; differences of TCD values between symptomatic and asymptomatic group were analyzed by *t* test; differences of characteristics inter groups were compared by χ^2 test. A *P* value of <.05 was considered statistically significant.

Results

TCD successfully identified all intracranial vessels. The mean degree of ICA stenosis was 89.2 ± 7.5%; the degree of stenosis was 70%–89% in 19 patients, 90%–98% in 33, and 99% in 8. Thirty-five patients (58.3%) had a contralateral ICA stenosis, 22 of them ≥70% (10 were occlusion). Ten patients (16.7%) had vertebral artery stenosis but only 5 were ≥70%. Forty-eight patients (80.0%) had adequate collateral flow supply. Immediate morbidity was low (6.6%), and only 2 TIA and 2 minor strokes were observed. There were no deaths, disabling strokes, or myocardial infarcts. Fifteen patients (25%) showed symptoms considered to be mild hyperperfusion symptoms early after CAS: headache in 9 and hypertension in 6. Symptoms resolved in 24 hours.

After CAS, TCD (mean time: 3.13 ± 1.34 hours) showed a significant MFV increase in the ipsilateral MCA and ACA and a significant MFV decrease in the ipsilateral PCA. On the contralateral side, a smaller but not significant MFV increase in the MCA and a significant MFV decrease in the ACA and PCA were found. PI increased in both MCA and ACA, but only significantly on the ipsilateral side (Table 2). In 16 patients without MFV increment in the ipsilateral MCA, a PI increment was found. Collateral supply from contralateral ICA and the external carotid artery, as reverse flow in the ipsilateral ACA and in the ophthalmic artery, disappeared immediately after CAS as the direction of the flow shifted to normal. Blood pressure values were 115.8 ± 21.6 over 64.3 ± 12.7 mm Hg.

At 30 days, TCD showed significantly lower velocities than

Table 2: Hemodynamic data immediately after CAS compared with pre-CAS values

Doppler Values	Ipsilateral		Contralateral	
	Pre-CAS	Post-CAS	Pre-CAS	Post-CAS
MCA-MFV	49.7 ± 16.8	62.5 ± 22.3**	51.3 ± 16.9	53.4 ± 16.6
MCA-PI	0.85 ± 0.18	1.09 ± 0.20**	0.99 ± 0.22	1.03 ± 0.22
ACA-MFV	50.7 ± 21.8	58.9 ± 23.0*	63.7 ± 22.7	50.3 ± 18.3**
ACA-PI	0.90 ± 0.22	1.08 ± 0.22**	0.96 ± 0.27	1.04 ± 0.23*
PCA-MFV	47.5 ± 21.0	36.5 ± 13.2**	45.3 ± 15.3	38.6 ± 17.3**
PCA-PI	1.01 ± 0.22	1.01 ± 0.21	1.00 ± 0.23	1.04 ± 0.22

Note:—CAS indicates carotid angioplasty stent placement; MCA, middle cerebral artery; MFV, mean flow velocity, cm/s; PI, pulsatility index; ACA, anterior cerebral artery; PCA, posterior cerebral artery.
* $P \leq .05$.
** $P < .01$.

Table 3: Pre-CAS data compared with post-CAS data 30 days later and *P* values; early post-CAS data compared with post-CAS data, at 30 days and *P* value (statistical significance)

Doppler values	Pre-CAS	Early Post-CAS	Post-CAS, at 30 days
iMCA-MFV	50.3 ± 17.0	63.0 ± 21.7	52.8 ± 15.6**
iMCA-PI	0.84 ± 0.19**	1.02 ± 0.22	1.12 ± 0.23**
iCVR	26.0 ± 17.3**		37.0 ± 22.0
cMCA-MFV	51.5 ± 17.4	54.1 ± 16.9	49.6 ± 16.9*
cMCA-PI	0.98 ± 0.23	1.03 ± 0.23	1.02 ± 0.26
cCVR	30.1 ± 18.2		33.5 ± 17.4

Note:—CAS indicates carotid angioplasty stent placement; i, ipsilateral; MCA, middle cerebral artery; MFV, mean flow velocity; PI, pulsatility index; CVR, cerebrovascular reserve; c, contralateral.
* $P < .05$.
** $P < .01$.

Table 4: Clinical and TCD data of patients with TIA/stroke after stenting

Patient No. Age in Years	Clinical Symptoms and Time Onset	Grade of Ipsilateral and Contralateral Stenosis and Plaque Characteristics	MFV, PI of Ipsilateral MCA before, Early after CAS, and 30 Days Later	Basal Ipsilateral CVR and 30 Days after CAS
1, 72	Minor stroke: right brachial and facial weakness, 12 hours after CAS	95% left ICA, 80% right ICA, 22 mm, ulcerated plaque	40 cm/s, 0.75 55 cm/s, 0.89 45 cm/s, 0.93	12.5% 13.3%
2, 81	Two TIAs: right hand weakness, 9 hours and 15 hours after CAS	95% left ICA, no contralateral stenosis, 20 mm, ulcerated plaque	37 cm/s, 1.27 49 cm/s, 1.59 55 cm/s, 1.24	7.6% 11.4%
3, 76	Minor stroke: pure verbal deafness during CAS	99% right ICA, no contralateral stenosis, 30 mm, ulcerated calcium plaque	42 cm/s, 0.86 38 cm/s, 1.45 44 cm/s, 1.41	19.0% 75%
4, 80	TIA: left hemineglect and anosognosia, during CAS	99% right ICA, 50% left ICA, 10 mm, nonulcerated plaque	23 cm/s, 0.87 29 cm/s, 1.10 24 cm/s, 1.08	0% 50%

Note:—TCD indicates transcranial Doppler; TIA, transient ischemic attack; MFV, mean flow velocity; PI, pulsatility index; MCA, middle cerebral artery; CAS, carotid angioplasty stent placement; CVR, cerebrovascular reserve; ICA, internal carotid artery.

those obtained immediately after revascularization, in both MCA. In the ipsilateral MCA, the PI increased from 1.02 ± 0.22 to 1.12 ± 0.23 ($P = .00$). No changes were observed on the contralateral side (Table 3). Blood pressure levels were significantly higher than those measured immediately after CAS: 140.1 ± 19.8 over 76.6 ± 11.5 mm Hg ($P = .00$).

When the values obtained on the 30-day control were compared with pre-CAS values, we found an increase of MFV and PI in the ipsilateral MCA, though only the PI increase was significant ($P < .05$). Few nonsignificant changes of MFV and PI were shown on the contralateral side (Table 3). Blood pressure values were similar to those values before CAS: 142.2 ± 19.6 over 76.4 ± 11.4 mm Hg (not significant).

After CAS, hemodynamic changes in both MCA were compared in patients with mild symptoms such as headache and hypertension ($n = 15$) and patients without those symptoms ($n = 41$). Increments of MFV and PI were observed in both groups. The group with headache and hypertension showed higher increments (ipsilateral MCA-MFV and PI, 50.5% and 39.3%, respectively; contralateral MCA-MFV and PI, 13.6% and 19.1%, respectively) than the asymptomatic group (ipsilateral MCA-MFV and PI, 24.3% and 27.3%, respectively; contralateral MCA-MFV and PI, 6.5% and 3.7%, respectively). These findings were not significant. Patients with TIA/minor stroke of probable thromboembolic mechanism showed TCD changes similar to those of asymptomatic patients, and they did not suffer hypertension or headache after CAS (Table 4).

CVR previous to CAS was normal in 40 patients (66.6%) and defective in 18. Two patients did not tolerate apnea. One month after CAS, CVR improved in both sides, with a significantly greater response on the operated side (from 26.0 ± 17.3% to 37.0 ± 2.0%) (Table 3). These changes were found in patients with and without previous normal CVR.

Discussion

The cerebral hemodynamic effects of CAS were evaluated in this study. TCD showed a significant MFV increase in both ipsilateral MCA and ACA immediately after CAS. These changes can be interpreted as an increase of the perfusion pressure as a consequence of the recovery of normal diameter and flow in the ICA after CAS. MFV, previously increased in both PCA and in the contralateral ACA as a compensating mechanism of the poor perfusion pressure in the affected hemisphere, decreased significantly immediately after CAS, reflecting the improvement of the cerebral hemodynamics. Similar results have been reported after CEA.[5-8] Although in our series and elsewhere[5,7,8] no significant changes were observed in the contralateral MCA, other studies have shown a moderate MFV increase related to the arrest of the crossflow through the anterior communicant artery after CEA.[6,28] Other CEA studies observed that patients who failed to show postoperative increase in contralateral MFV-MCA had severe stenosis of the contralateral ICA and a chronic hypoperfusion of that hemisphere.[7] In our series, nearly 60% of patients had contralateral ICA stenosis.

PI also increased in MCA bilaterally and in the ipsilateral ACA immediately after CAS. This change showed the capability of constriction of the resistance arterioles to withhold the important increase of flow that occurred in the ICA territory after CAS.

Besides these findings observed in 73.3% of our patients, 16 patients (26.7%) showed no changes or even a decrease of MFV after CAS, despite a PI increase in both MCA and the ipsilateral ACA. This finding could be explained by an overfunction of the resistance arterioles to avoid the consequence of the abrupt increment of perfusion pressure that may occur after CAS. The decreased MFV could be the result of this early vasoconstrictor autoregulation mechanism reflected in the high PI. These results point out that the PI increase should be considered a more sensible marker of hemodynamic changes than the MFV, and it is indicative of hemodynamic improvement. These patients showed no significant differences in demographic data, degree of carotid stenosis, number of collateral vessels, basal CVR, and periprocedural complications with respect to the other patients. In addition, another series of patients undergoing CEA have revealed that PI of MCA is a better predictor of the risk or hyperemia and stroke during and after operation.[29]

A MFV increase together with a PI decrease in the ipsilateral MCA, after CEA, has also been reported.[26,30] These studies included patients with headache or high blood pressure and high TCD velocities or even a complete HS early after CEA. In all these patients, decreases of PI indicate a refractory vasodilation state deriving from an impaired basal CVR, so that there is not an adequate response to the high perfusion pressure result of recanalization of ICA. When blood pressure was controlled, a clinical remission and normalization of TCD values occurred. In our series, patients with headache and hypertension after CAS[15] showed more pronounced postoperative increases in PI and MFV of MCA than patients without postoperative hypertension and headache, though this difference was not significant. Four of the patients with headache and hypertension had an increase only of PI, with no changes of MFV, whereas 3 showed increments of ipsilateral MFV $\geq$ 100% without PI increase. None of them developed a complete HS,[12] and symptoms resolved in less than 24 hours with control of blood pressure. In the asymptomatic group, there were 3 patients with increments of ipsilateral MFV $\geq$ 100%.

Therefore, our data indicate that revascularization effects are not homogeneous and that 4 different situations can be found after CAS: 1) patients with PI increase only, asymptomatic; 2) patients with MFV and PI increases, again asymptomatic; 3) patients with higher MFV and PI increases and hyperperfusion TCD criteria,[31,32] but asymptomatic; and 4) patients with higher MFV increase, but without changes or even decrease of PI. The latter may have mild self-limited hyperperfusion symptoms or may develop a complete HS. These patients should be monitored closely with a stricter control of blood pressure and serial neurologic examinations to prevent complications.

The morbidity of our series was very low, and no patients died or had disabling stroke or myocardial infarction. Only 2 patients had TIA and 2 other minor stroke immediately after CAS. Although we cannot make any conclusions, these 4 patients had severe stenosis with large ulcerated plaques, impaired basal CVR, and were older than 70. None of them had headaches, hypertension, or other symptoms of HS afterward. The hemodynamic changes they showed early after CAS were similar to the most common pattern of ipsilateral MCA increase of both MFV and PI. Although cerebral protection was used during the CAS procedure, a thromboembolism mechanism can be suspected. Occlusion time was less than 10 seconds according to our CAS protocol, and any particle less than 100 μm crossing the pore size of the filter could have been responsible for the occlusion of a distal artery. In addition, all of them had severe impairment of cerebral reserve before CAS, which may have influenced the development of complications. Despite the mild symptoms, they presented a clear benefit from CAS as they showed an improvement of hemodynamics reflected in both higher PI and MFV in the ipsilateral MCA than basal values, and a normal CVR 30 days later (Table 4).

At 30 days after CAS, the early increment of MFV observed in the ipsilateral hemisphere was maintained although minor, indicating a progressive normalization of ipsilateral cerebral hyperemia occurring immediately after CAS. This value was higher than basal MFV, which indicates an improvement of cerebral perfusion. PI increment was progressive during the first month, and was shown in both hemispheres, though significant only in the ipsilateral MCA. This indicates a vasoconstrictor response of resistance arterioles to the earlier hyperemia in response to re-established unilateral perfusion and the restoration of autoregulation mechanisms. Different CEA studies have observed similar delayed postoperative hemodynamic changes. A longer follow-up of 3 to 12 months revealed a progressive normalization of parameters with an improvement of hemodynamics in most patients.[6,10,12]

One limitation of our study was that CVR was not evaluated immediately after CAS. We could not obtain sufficient collaboration from patients to make apnea, and also we preferred to clarify hemodynamic results immediately after CAS. However, we assessed CVR 30 days after CAS and observed increments of CVR with respect to preoperative values, indicating a global cerebral CVR improvement after CAS that was

more marked on the ipsilateral side. In addition, those patients with impaired preoperative CVR (33.4%) normalized in the chronic stage.

In summary, CAS improved global cerebral perfusion and CVR as TCD values indicated. Early after CAS, most patients show increases of MFV and PI, reflecting an increment of perfusion pressure and an adequate vasoconstrictor response of arterioles. This hemodynamic improvement is maintained 30 days later because of a higher PI and a better CVR with respect to basal values, respectively. This degree of improvement is similar to that seen after CEA. In addition, the PI seems to be a better marker of cerebral hemodynamics. A lower PI after CAS may indicate persisting vasodilation and impaired cerebral reserve, which could led to an HS. Therefore, there is a profile of MFV/PI changes that would increase a patient's odds of developing subsequent clinical events after stent placement. Early detection of this condition by TCD may avoid serious complications. In addition, the study of CVR previous to CAS may help to identify those patients at risk of periprocedural complications.

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