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Brief Report
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Short and Long-Term Effect of Carotid Artery Stenting on Arterial Blood Pressure Measured through Ambulatory Blood Pressure Monitoring

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Background: The aim of this study was to assess the short and long-term effects of carotid artery stenting (CAS) procedure on blood pressure (BP) through ambulatory BP monitoring.

Methods: One hundred fifty three patients who underwent CAS for primary or secondary protection from December 2010 to September 2013 were enrolled to our study. The BP levels of total of 123 patients were monitored for 1 year. Thereafter, the pre-procedure levels of BP were compared with BP levels at the 24-hour and the first year intervals after the procedure.

Results: Systolic and diastolic BP levels at the 24-hour and the first year intervals after CAS were significantly lower than the pre-procedure BP levels. The mean 24-hour systolic BP was 113 ± 13 mmHg and diastolic BP was 63 ± 8 mmHg, both of which were significantly lower ($p < 0.001$ and $p < 0.001$ respectively), while the pre-procedure mean systolic BP was 133 ± 10 mmHg and the mean diastolic BP was 75 ± 9 mmHg. Moreover, the mean first-year systolic BP was 125 ± 10 mmHg with a decline of 8 ± 8 mmHg and mean diastolic BP was 71 ± 8 mmHg with a decline of 4 ± 7 mmHg, both of which were again significantly lower compared to the pre-procedure levels ($p < 0.001$ and $p < 0.001$ respectively).

Conclusions: The results of our study suggested that systolic and diastolic BP levels diminished after CAS. Additionally, BP reduction continued even 1 year after the CAS.

Key Words: Ambulatory BP monitoring • Carotid artery stenosis • Carotid artery stenting • Carotid sinus baroreceptor • Stroke

INTRODUCTION

Carotid artery stenosis is a major cause of neurologic morbidity and mortality.[1] Carotid artery stenting (CAS) is a suitable alternative to carotid endarterectomy (CEA) in patients with carotid artery stenosis since it is less invasive and does not require general anesthesia.[2]

Arterial hypertension is a modifiable risk factor that is recognized as a major cause of both ischemic and hemorrhagic stroke.[3] Baroreceptors located in the arcus aorta and carotid sinus bifurcation play a significant role in regulating blood pressure (BP). Immediately after carotid artery stenting, arterial hypotension caused by stent compression on the carotid sinus baroreceptor is a common hemodynamic alteration.[4,5] However, current data in the literature regarding the long-term alterations in BP after CAS are limited.[6,7]

It is imperative to follow systemic BP regularly in patients with carotid artery disease. Arterial BP measure-

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ment is influenced by the knowledge of the person measuring it, including factors such as use of manual or automated blood pressure measurement device, calibration of the device, positioning of the body, fasting state of the patient, and the time of the measurement. Therefore, ambulatory blood pressure measurement devices are used in order to minimize these elements and generate reliable readings.[8]

The aim of this trial was to assess the effects of CAS procedure on BP at the 24-hour and first year intervals after the procedure through ambulatory BP monitoring.

MATERIALS AND METHODS

Study population

In this prospective study, we enrolled 155 patients who underwent CAS from December 2010 to September 2013. The local Ethics Committee of our institution approved the study. All patients were followed clinically and radiologically for a year, and the inclusion criteria for patients to receive CAS treatment were > 50% stenosis in the carotid artery as assessed by angiography in a symptomatic patient, or > 70% stenosis in the carotid artery as assessed by angiography in an asymptomatic patient. The exclusion criteria included the presence of heart failure, severe respiratory insufficiency, renal failure, severe arrythmia, cerebral bleeding, resistant hypertension, and patients with restenosis of carotid stent who did not take their medications regularly, had problems with insomnia, used vasodilators for indications other than hypertension, and experienced a complication during the CAS procedure.

Percentages of carotid artery stenosis were calculated according to the NASCET criteria. Patients who had ischemic cerebrovascular event, transient ischemic attack (TIA), or amaurosis fugax with or without sequela within the past 6 months were defined as symptomatic patients. Restenosis was diagnosed when instant peak flow velocity was ≥ 224 cm/s in Doppler ultrasound or ≥ 50% stenosis was present in CT angiography.

Ambulatory BP monitoring

Ambulatory BP monitoring (ABPM) studies were performed by using a Mobil-O-Graph NG, I.E.M GmbH, Stolberg Germany) monitoring device. Patient BP was measured by oscillometric method and the first-hour value was excluded from the analysis. BP readings were obtained automatically at 15-min intervals during the day, and at 30-min intervals during the night. All measurements were performed on the left brachial artery. Recordings were accepted only if more than 85% of the raw data were valid.

After CAS procedure, patients were clinically and radiologically followed at the 1st, 3rd, 6th and 12th months. Systolic and diastolic BPs were monitored 24 hours before, 24 hours after and at the 1st year of the procedure through ABPM. Patients were assigned to undergo the CAS procedure after their BP regulation was performed. At each visit, manual BP recordings of patients from the previous week were also analyzed and their antihypertensive treatment was evaluated. Twenty-four hour Holter BP monitoring was performed for patients who did not have regulated arterial BPs. Patients who had persistent hypertension during the follow-ups were given increased doses or an additional antihypertensive medication. The number of antihypertensives or the dose of the medication was reduced in patients who had symptomatic hypotension.

Carotid angioplasty and stenting

All CAS procedures were performed via transfemoral access with local anesthesia in a single center and by the same team. All patients received 100 units/kg intravenous unfractionated heparin bolus prior to the procedure. Carotid artery lesions with > 90% occlusion were treated with balloon angioplasty prior to stenting. Balloon postdilatation at > 8 atm was performed for all lesions. A 1-mg intravenous atropine was given to all patients who had a pulse rate under 50 beats/minute after balloon angioplasty. A residual occlusion of < 30% after CAS and balloon postdilatation procedure was considered to be a successful criterion. A very low number of patients who had a residual occlusion of > 30% after balloon postdilatation were excluded from the study. Self-expandable stent was preferred for carotid stenting, and an embolism protection device was used in all procedures. Oxygen saturation and arterial BP of the patients were monitored during the procedure. Bidirectional cerebral angiography was performed to demonstrate intracranial segments before and after CAS. Bilateral carotid artery stenosis was present in 22 patients

(18%). Nine patients (7%) had total occlusion of contralateral carotid artery. In patients with significant bilateral carotid stenosis, primary intervention occurred on the symptomatic lesions, whereas the lesions with worse prognosis were principally treated in asymptomatic patients and intervention for contralateral lesions occured one month later. All patients were tested for aspirin and clopidogrel resistance one day before the procedure.

Statistical analysis

Data were analyzed with the SPSS software version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequency and percentage. The $\chi2$ test and Fisher's exact test were used to compare the categorical variables, and the Kolmogorov-Smirnov test was used to assess the distribution of the continuous variables. Student's t-test was used for variables with normal distribution and the values were presented as mean $\pm$ SD. The paired t-test was used for same variables before and after stenting. Wilcoxon signed rank test was used for non-parametric variables before and after stenting. For categorical variables McNemar's test was performed before and after stenting. Multivariate regression analysis was used to evaluate the independent associates for BP decrease. The odds ratios (OR) and 95% confidence intervals (CI) were calculated. A two-tailed p-value of < 0.05 was considered statistically significant.

RESULTS

Of the total 155 patients that were enrolled in the study, 32 were excluded due to inadequate 1-year follow-up; of those 32 patients, 5 were not regularly taking their antihypertensive medications, 6 had their anti-hypertensive changed due to side effects, 7 had irregular ambulatory BP Holter recordings, 2 had acute CAS thrombosis, 3 had carotid stent restenosis, 1 had myocardial infarction, 1 had renal failure, 1 had gastrointestinal bleeding, 5 were lost to follow-up and 1 died. Therefore, the study was completed using statistical analysis on 123 patients (Figure 1), of whom 97 were men (79%).

The mean age of the patents enrolled in the study was 68 $\pm$ 9. Of the total enrolled patient population and after exclusions, 79% were male, 84% of the study participants had hypertension, 87% had coronary artery disease, 43% had type-2 diabetes mellitus, 68% had hyperlipidemia, and 40% had a history of smoking. In our study group, 75% of the patients were symptomatic for ischemic cerebrovascular events. The restenosis rate 1 year after CAS was 2.5%. To protect against embolism after CAS, the proximal blockade system and the distal embolus prevention method were used in 59% and 41% of patients, respectively. Demographic features, clinical and angiographic findings of our patients are summarized in Table 1.

After all patients had been evaluated subsequent to undergoing CAS procedure, there was a significant reduction in both systolic and diastolic BPs at the 24 hour and 1 year intervals when compared to the levels before the procedure. The mean systolic BP before CAS procedure was 133 $\pm$ 10 mmHg; 24 hours after the operation, the mean systolic BP fell from 20 $\pm$ 12 mm Hg to 113 $\pm$ 13 mmHg. The decrease in systolic BP was statistically significant ($p < 0.001$). The mean diastolic BP before CAS procedure was 75 $\pm$ 9 mmHg, and the mean diastolic BP after the operation decreased from 13 $\pm$ 9 mmHg to 63 $\pm$ 8 mmHg. The decrease in diastolic BP was statistically significant ($p < 0.001$). The mean systolic BP at the 1^{st} year after CAS procedure was 125 $\pm$ 10 mmHg with a reduction of 8 $\pm$ 8 mmHg when compared to the baseline levels. The decrease in systolic BP was also statistically significant ($p < 0.001$). The mean diastolic BP at the 1^{st} year after CAS procedure was 71 $\pm$ 8 mmHg with a reduction of 4 $\pm$ 7 mmHg when compared to the baseline levels. The decrease in diastolic BP was statistically significant ($p < 0.001$) (Table 2).

An important finding of our study was that CAS reduced the number of antihypertensive medications taken by the patients. The mean number of antihypertensives taken by the patients prior to CAS was 1.6 $\pm$ 0.8 while it was reduced to 1.5 $\pm$ 0.8 at the 1^{st} year following CAS. Such reduction in the mean number of antihypertensives was statistically significant ($p = 0.009$). Regarding the categories of drugs, the proportion of beta-blockers, RAAS blockers, diuretics, dihydropyridine calcium channel blockers and nonhydropyridine calcium channel blockers (%) was 56, 48, 27, 24, 6, respectively, before CAS. They fell to (%) 50, 49, 23, 22, and 5, respectively, at the first year following CAS. Among the anti-

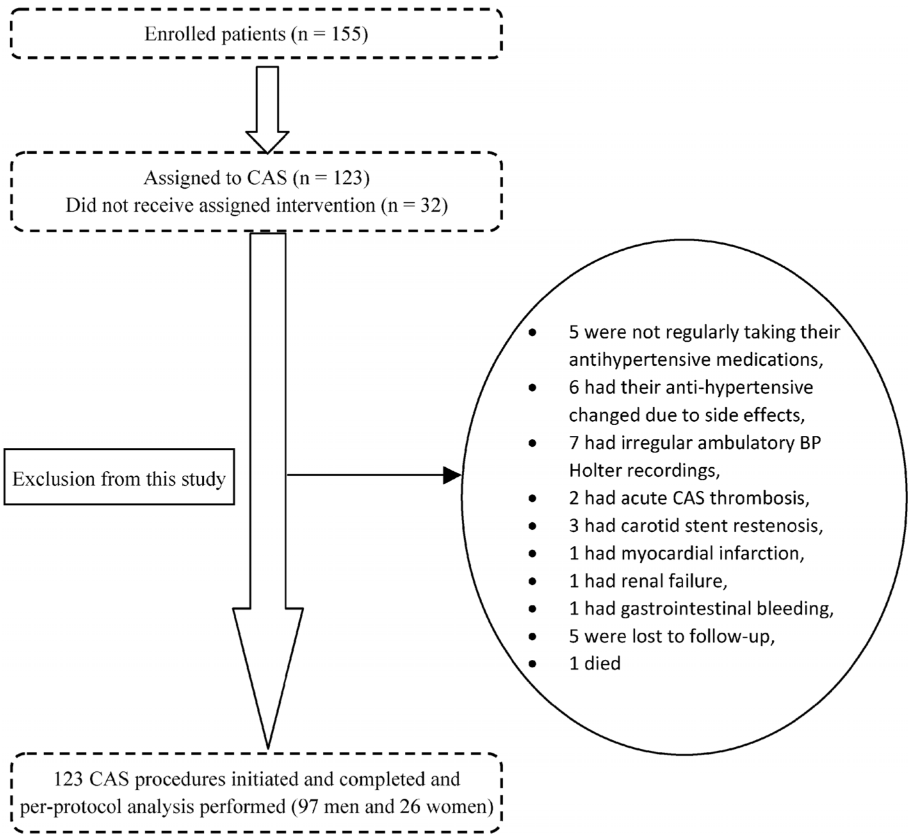

Figure 1. *Flow of patients. BP, blood pressure; CAS, carotid artery stenting.*

Table 1. Demographic characteristics, clinic and angiographic findings

Parameter	
Mean age (yrs)	68 ± 9
Gender, male (%)	79
Hypertension (%)	84
Type 2 diabetes mellitus (%)	43
Coronary artery disease (%)	87
Hyperlipidemia (%)	68
Smoking (%)	40
Symptom present (%)	75
Bilateral ICA stenosis (> 70%) (%)	18
Opposite side ICA 100% occluded (%)	7
Restenosis rate (%)	2.5
Proximal blockade sysyem (%)	59
Distal embolus prevention (%)	41

ICA, internal carotid artery.

hypertensives, RAAS blockers had an increase of 1% at the 1st year following CAS while the others showed a reduction. A full 6% reduction in the use of beta-blockers was statistically significant (p = 0.016), although reductions in the other antihypertensive drug categories were not statistically significant (Table 3).

Table 2. Blood pressure changes at first 24 hour interval and at first year after CAS procedure

Blood pressure mmHg	Before CAS	24 hour after CAS	p value	First year after CAS	p value
SBP	133 ± 10	113 ± 13	p < 0.001	125 ± 10	p < 0.001
DBP	75 ± 9	63 ± 8	p < 0.001	71 ± 8	p < 0.001

CAS, carotid artery stenting; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Multivariate regression analysis was performed for both systolic and diastolic BP in order to assess the effects of patients' demographic features, comorbid disease, change in the body mass index, whether carotid artery plaque was symptomatic, change in the number of antihypertensives taken for 1 year, size of the balloon used in CAS and whether the stent was an open-closed cell on BP levels at the first year. The analysis revealed that no other variables except CAS procedure had a sig-

Table 3. Number of antihypertensives taken by patients before CAS and at the 1st year after CAS and changes in the drug categories

Categories and number of antihypertensive drugs	Before CAS	At 1st year after CAS	p value
Beta blockers (%)	56	50	0.016
RAAS blockers (%)	48	49	1.00
Diuretics (%)	27	23	0.18
Dihydropyridines CCB (%)	24	22	0.45
Nondihydropyridines CCB (%)	6	5	1.00
Mean number of medications (n)	1.6 ± 0.8	1.5 ± 0.8	0.009

CAS, carotid artery stenting; CCB, calcium channel blocker; RAAS, renin-angiotensin-aldosterone system.

nificant effect on the reduction of BP levels (Table 4).

Those patients who had a peak heart rate of < 50/min after CAS were given 1 mg atropine during the procedure. No bradycardia that required pace after the procedure was observed. We had 1 patient with hypotension that required ionotropic support after the procedure. That patient was not included in the study due to carotid artery stent thrombosis. No other patients had hypotension requiring ionotropic support.

DISCUSSION

In this study, we demonstrated that patient BP levels at the 24-hour and the 1 year intervals after CAS procedure were significantly lower in our study group. ABPM evaluation of the BP changes led to more objective results. These results are promising since the decrease in BP obtained after CAS procedure might play a role in the prevention of stroke during long-term follow-up.

The efficacy of CAS in primary and secondary prevention of ischemic stroke has been previously demonstrated.[9] During and after the CAS procedure, hemodynamic instability might be observed.[5,10-13] The frequency of hypotension after CAS procedure was reported to range from 18.8 to 56.1%.[4,14] In the Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis (EVA-3S) study, 11 out of 261 patients (4.2%) with symptomatic carotid artery stenosis had hypotension and bradycardia, which persisted for 30 days after the procedure.[15] It is widely accepted that hemodynamic instability after CAS procedure is due to stretching of the carotid sinus baroreceptors due to the stent.[16] Carotid sinus arterial wall thickness is thinner when compared to the other arteries with the same calibration. Stimulation of the adventitial baroreceptors through stent leads to the inhibition of sympathetic neurons in nucleus tractus solitarius. This inhibition decreases the sympathetic tonus on the peripheral vessels, thus the systemic BP decreases. The carotid stents that we used in our study

Table 4. Independent predictors of reduction in systolic and diastolic blood pressure at the 1st year in multivariate regression analysis

	Standardized coefficients	t	95% Confidence interval		p
	Beta		lower	upper	
Stent location	-0.01	-0.13	-1.85	1.63	0.90
Balloon size	-0.11	-1.15	-2.57	0.68	0.25
Body mass index	0.03	0.33	-0.54	0.75	0.74
Stent type	0.12	1.21	-1.00	4.14	0.23
Change in the number of antihypertensive medications	0.04	0.36	-1.29	1.86	0.72
Symptomatic	-0.08	-0.83	-2.43	0.99	0.41
Age	-0.02	-0.15	-0.16	0.13	0.88
Sex	0.13	1.25	-1.20	5.31	0.21
Hypertension	0.01	0.10	-3.33	3.67	0.92
Diabetes mellitus	0.06	0.51	-2.09	3.52	0.62
Coronary artery disease	0.05	0.49	-0.84	1.40	0.62
Hyperlipidemia	0.11	1.06	-1.27	4.18	0.29
Smoking	-0.15	-1.54	-4.64	0.59	0.13

were self-expandable Nitinol stents. These self-expandable stents take the shape of the arterial wall after 6 months to 1 year and attach to the wall more easily. Therefore, the stent causes chronic mechanical pressure on the carotid sinus baroreceptors.[9] This mechanism might play a role in persistent decrease in BP. Similarly, in patients who underwent surgery, the pressure on the baroreceptors due to hematoma and edema in the early term may cause a drop in BP; however, when this pressure is relieved in the long-term, the BP levels might return to their pre-operative values.

As intima-media thickness of the carotid increases, baroreceptor sensitivity of carotid decreases.[17] Atherosclerosis and hypertension leads to thickening of the carotid sinus, which renders it more resistant to deformations and decreases the baroreceptor sensitivity.[6] The higher number of patients with hypertension and coronary artery disease in our study might have prevented further decrease in BPs after CAS procedure.

After researchers demonstrated a higher risk of distal embolization after percutaneous intervention when compared to CEA that might lead to neurologic deficits, cerebral protection devices are currently used. As an embolism prevention method during CAS procedure, distal embolism protection filters and a proximal blockage system are used. Studies investigating hemodynamic alterations in CAS procedures usually used a distal embolism protection filter. In our study, 59% of patients had a proximal blockage system as a cerebral embolism protection method. This study differs from its previous counterparts with this unique feature.

Patients who had post-dilatation CAS procedure had a higher frequency of hypotension during the short-term follow-up.[18] In this study, all patients had > 8 atm balloon post-dilatation after CAS procedure. The balloon post-dilatation procedure helps to provide improved alignment of the stent in the carotid artery wall, but the pressure exerted on the carotid sinus increases. We found higher levels of decrease in BP at the 24th hour after the procedure when compared to the BP decreases at the 1st year. This might be attributed to the balloon post-dilatation procedure performed immediately after the stent placement.

No life style changes were recommended to the patients after CAS. No significant change was found in the body mass index of patients at the first year. It was important to reveal whether the other characteristics of the patients had an effect on the reduction of BP in the first year following the CAS. The analysis performed for that purpose demonstrated that the comorbid diseases, a slight change in body mass index, reduction in the number of antihypertensive medications, and the diameter of balloon and type of stent used in CAS did not have an effect on the reduction of BP levels in year 1 after CAS.

A statistical reduction was observed after CAS in the number of antihypertensives taken by the patients. The reduction was more marked in the beta-blockers because the peak heart rate may also decline in addition to BP when the baroreceptors are stimulated by the stent. The number of RAAS blockers taken by the patients increased slightly at the first year interval following CAS because a significant number of our patients had coronary artery disease or diabetes mellitus. Therefore, the RAAS blockers were not given priority when the number of antihypertensives of the patients would be reduced.

In previous treatment studies in which electrical carotid sinus stimulation was performed for resistant hypertension, the electrodes were placed on bilateral carotid arteries. In 2012, Hoppe et al. used a new electrode called Barostem neo placed on the unilateral carotid artery. An average of 26/12 mmHg reduction was observed in the BP levels for 6 months in the study in which Barostem neo electrodes were used.[19] The findings of this study are comparable to those of the DEBUT-HT trial in which the electrodes (Rheos system) were implanted on bilateral carotid artery.[20,21] Joonho et al. studied the short and long-term effects of carotid endarterectomy and carotid stenting procedure on BP; a full 95.3% of the patients undergoing CAS and 93.2% of patients undergoing CEA had unilateral carotid lesions.[22] Therefore, unilateral carotid sinus stimulation also decreased the BP. The unilateral stenting rate in our study was 82%.

The risk of having recurrent stroke in a patient who has a history of TIA or stroke ranges from 6% to 12% in 1 year and from 40% to 50% in 5 years. These numbers highlight the importance of controlling the risk factors including atherosclerosis and hypertension, which are major causes of stroke. BP control is critically important in the primary and secondary prevention from stroke. It is well-known that even small decreases in BP might decrease the risk of stroke tremendously.[23] In the PROGRESS study, a 9/4 mmHg decrease in BP in patients who had a history of cerebrovascular accident decreased the risk of stroke by 28%.[24] Our results are parallel to the current literature and CAS procedure decreased the BP both at the short-term and at the 1st year interval after the procedure. One year after the CAS procedure, the decrease in systolic and diastolic BPs was 8 ± 8 mm Hg and 4 ± 7 mm Hg, respectively, which we believe will substantially decrease the long-term stroke risk.

Limitations of the study

In this study, there were limitations. We did not record the durations of the procedures, which might have affected the early BP readings. Since most of our patients were male, the results might not be valid in a female population. Life style changes were not recommended to the patients who underwent the CAS procedure. The absence of a control group was also a limitation of our trial.

CONCLUSIONS

Our study found that systolic and diastolic BPs decrease after CAS procedure. This decrease in BP is also maintained after 1 year. This decrease in BP after CAS procedure may provide additional benefit to decrease the stroke risk in this patient group.

DISCLOSURES

The authors declare that they have no conflict of interest.

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